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On behalf of all of us in FBIS I wish to express appreciation to our readers who have guided our efforts throughout the years.

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CHEMICAL PROTECTION AGAINST HIGH-ENERGY PROTON RADIATION

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[Article by Ye. I. Vorob'yev, V. I. Yefimov, V. S. Shashkov and A. V. Sedov,
submitted 14 Jan 80]

[English abstract from source] Comparison of chemical protection against electromagnetic radiations (X- and γ -rays) and high-energy proton radiations give evidence that the mechanism of antiradiation effects of radioprotectors and other biological protectors against different radiations is identical. On the basis of the data published in the literature it has been shown that the degree of radiation protection of animals and other biological objects in comparable doses differs insignificantly during exposures to proton and standard irradiations.

[Text] In the late 1950's, the problem of studying biological effects of cosmic radiation on organisms emerged in connection with the start of exploitation and man's exploration of space (1961). High-energy protons contained in galactic cosmic radiation, earth's radiation belts, as well as proton particles with energy of tens of gigaelectron volts, which are generated when there are chromospheric solar bursts, present a probable radiation hazard to man and the biological element of life support systems during space flights. This circumstance made it imperative, not only to study the biological effects of protons as components of cosmic radiation, but to search for means of protection, including chemical ones, against high-energy protons.

Soviet scientists are unquestionably in the lead in the area of research to modify the radiobiological effects induced by proton radiation. Experimental studies dealing with chemical prevention of this form of radiation injury in various biological objects have been pursued in our country since the early 1960's, virtually concurrently with the study of the biological effects of protons varying in energy. Already in the earliest studies of S. P. Yarmonenko et al. [1-3] it was shown that the radioprotective effect of the best known thiol (cystamine, β -mercaptoethylamine--MEA, aminoethylisothiuronium--AET) and amine (serotonin, mexamine) protective agents used in mice exposure to 660 MeV protons in a dosage of 950-1100 rad was quite commensurable with the protective effect of the same agents with exposure to x- and γ -rays in comparable doses (700-800 R). It was noted that there was attenuation of the effect of amine protective agents with increase in dosage of proton radiation to 1500-1550 rad, as in the case of standard radiation.

Subsequently, experiments on mice [4-7] and rats [8-12] revealed that the efficacy of agents with radioprotective action against acute exposure to 660-MeV protons was entirely retained with exposure to protons with energy of 510, 220 and 120 MeV.

American authors [13], who tested paraaminopropiophenone (PAPP) on mice exposed to 150-400 MeV protons, discovered that the radioprotective action of this agent depended little on proton energy with doses of 700-900 rad. In another comparative study of MEA and PAPP [14] on mice, it was shown that the dose reduction factor (DRF) was somewhat higher for MEA than PAPP (1.61 and 1.39, respectively) after exposure to 440-MeV protons over a wide range of doses (200-1800 rad). Preventive administration of adeturon to mice exposed to 645-MeV protons in a dosage of 700-800 rad resulted in over 90% survival, versus absolute death of control mice. All of the treated animals survived with delivery of 600 rad ($LD_{70/30}$) radiation. The protective effect of adeturon was also demonstrated in experiments on rats and monkeys exposed to protons or γ -rays [15]. Unfortunately, the irradiation conditions were not described in the last cited work.

Cytological examination of bone marrow of mice exposed to radiation from 660-MeV protons after administration of AET revealed that this agent attenuated radiation induced degeneration of medullary cells. There were fewer cells with structural damage to chromosomes in protected animals than in the control, while the mitotic index was higher for the first 4 postradiation days [16]. Analogous protection of myelokaryocytes was demonstrated after giving mexamine to mice [17]. A similar degree of changes in hemopoietic organs is inherent in thiol and amine radioprotective agents with the use of standard electromagnetic forms of radiation [18].

Yu. G. Grigor'yev et al. [19] demonstrated a distinct radioprotective effect on bone marrow cells when mice were given MEA before exposure to 50-MeV protons in doses of 100-1000 rad. In mice given adeturon (660-MeV protons, dosage 600-800 rad), the protective effect of the agent was confirmed by the increase (as compared to the control) in number of endogenous colony-forming units (CFU) in the spleen.

Since the combined use of protective agents presumably having different points of application of their action is one of the promising methods of chemical protection, in order to obtain a high radioprotective effect when an organism is exposed to ionizing radiation, some combinations were also tested on animals exposed to protons. A high protective effect was demonstrated with the combination of mexamine and MEA, hydroxylamine and mexamine, AET or cystamine [1-3, 20, 21]. With the combined use of MEA and mexamine or serotonin, there was 50-53% survival of mice exposed to protons in doses of 950-1000 rad, versus only 10-30% survival with the use of these agents separately. There were substantially fewer myelokaryocytes with chromosomal aberrations in animals given MEA and mexamine, than with separate use of these agents [18]. A. G. Konoplyanikov et al. [7], who exposed mice to protons in a dosage of 1350 rad and used a preventive combination of MEA and serotonin, as well as prescriptions containing MEA, AET, reserpine or alcohol, obtained an appreciable increase in animal survival, as compared to administration of these agents individually. In rats exposed to 510-MeV protons in a dosage of 500 rad, the changes in the blood system were less marked when they were given cystamine with amygdalin than in animals given cystamine, mexamine, serotonin or PAPP separately [8]. Some interesting data were published by B. L. Razgovorov et al. [22], who showed that the combined use of cystamine and AET, even in low doses (50 mg/kg each), elicited over 50% survival among rats exposed to high-energy protons in doses of 750-1100 rad and 37% survival with doses of 1100-1300 rad.

Quite a few convincing facts have been accumulated to date concerning the use of protective agents, not only for animals, but other biological objects *in vivo* and *in vitro*, with exposure to protons varying in energy. Already the earliest experiments in this direction dealing with comparative studies of attenuation of the effects of γ - and proton radiation in haploid and diploid yeast cells by means of anoxia and over 20 protective agents referable to various chemical compounds revealed that there was virtually identical protection of cells exposed to 660-MeV protons and γ -rays with the use of the same protective agents. With both forms of radiation, the DRF differed little or were the same. A maximum protective effect was observed under the influence of anoxia, glycerin and thiol protectors [21]. Ye. A. Krasavin [23] submitted some convincing data on protection of *E. coli* and hydrogen bacteria by MEA and polyhydric alcohols (glycerin and inositol). According to his data, the DRF constituted 2.1-2.8 in the case of exposing bacteria to γ -rays and even somewhat higher (unreliably), 2.2-3.7, with exposure to protons of 640 MeV. It was demonstrated that when cystamine was added to a culture of lysogenic bacteria prior to irradiation there was a distinct attenuation of radiation induction [24]. It has been reported that MEA and citrophos (cysteamine adenosine triphosphate) have a radioprotective effect on transforming DNA when exposed to 645-MeV protons *in vivo* and *in vitro* [25].

The modification of radiation lesions to the corneal epithelium of mice and efficacy of chemical protection as a function of linear energy transfer (LET) were analyzed comprehensively by S. V. Vorozhtsova [26]. Mice were given intraperitoneal injections and applications to the eyes of an MEA solution prior to total-body "eye-side" exposure to protons of 645, 50 and 25 MeV, fast carbon ions or x-rays (180 kV). Use of this protective agent consistently led to reduction of aberrant mitoses in the corneal epithelium, which were induced by protons of the tested energies and x-rays. The DRF constituted 1.1, 1.3, 2.0 and 1.2 24 h after giving MEA and irradiation with protons of 645, 50, 25 MeV and x-rays, respectively. At the same time there was no protection when the cornea was exposed to heavy, fast carbon ions.

The results of this study indicate that chemical protection against corpuscular radiation of protons is related to the LET. The radioprotective action of radioprotective agents extends over the range of 25-640 MeV protons to virtually the same degree, and their LET is close to the corresponding values of hard electromagnetic radiations. The radiation lesions induced by proton radiation on the molecular and cellular level are virtually identical to the ones caused by standard radiation, while the radioprotective effects of protectors are quite comparable under these conditions. At the same time, high LET values of corpuscular radiation of heavy ions (thousands of megaelectron-volt-grams/cm²) are the cause of inefficacy of radioprotective agents due to a different mechanism of radiation damage to the object.

As yet, there is little information about alteration of long-term effects of proton radiation. S. P. Yarmonenko and V. N. Ivanov [27] made a study of surviving male rats given various protective agents (MEA, cystamine, AET, mexamine, hydroxylamine) or combinations thereof against 660-MeV protons in doses of 1300-1600 rad. There was virtually complete restoration of reproductive capacity of protected mice 4-7 months after irradiation. No appreciable effect of radiation was demonstrated with the preventive administration of chemical protective agents on the mean number of first-generation offspring from mating with healthy females. It was also reported that the use of mexamine combined with MEA elicited an analogous effect in mice exposed even to a dose of 1900 rad. These authors stressed that

the objectives of their work did not include the study of genetic sequelae. In another study [28], mice exposed to 600-MeV protons in doses of 600-1300 rad and given mexamine were followed up for the rest of their lives (1.8-2.3 years). A dynamic record was kept of body weight, graying and time of death. In the opinion of these authors, the degree of protection, though it was somewhat less marked than against the early postradiation sequelae, was distinct at the long term (according to weight gain and degree of graying of their fur). The life span of protected mice that survived acute radiation sickness was longer than that of the corresponding control animals. D. Ya. Oparina [29], who tested the attenuating effect of protective agents on tumor formation at the long postradiation term in female rats exposed to 645-MeV protons in single doses of 200 and 400 rad after being given MEA, prodigiosan or a combination thereof, kept the animals under observation for 2 years. Administration of MEA or combination thereof with prodigiosan led to a reliable increase in latency period of tumor formation, as well as lowering of breast tumors. However, administration of prodigiosan alone did not have a reliable effect on the incidence of neoplasms after exposure to protons. These results led the author to voice the opinion that the aminothiols protector has antitumorigenic effects when an organism is exposed to high-energy protons. The data in the literature to the effect that protective agents attenuate the long-term effects of x- and γ -rays [18, 30-35], as well as the results of studies described above, warrant the assumption that there is quite similar attenuation of long-term sequelae of irradiation in both species of animals.

Considerable information has been published in the literature concerning the use of radioprotective agents on large laboratory animals (in particular, dogs) exposed to high-energy protons. Evidently, this can be explained by the limited efficacy of known protective agents and dissimilarity of results obtained in experiments using standard forms of radiation on these animals [36]. Experiments were conducted to determine the biological effects of high-energy protons on dogs. The results showed convincingly (as did experiments on rodents) that the manifestations of the radiation syndrome induced by high-energy protons and standard types of radiation (in comparable doses) were completely identical in these animals. Consideration was given to indicators of survival, lesions to hemopoietic and other systems, pathomorphological findings and long-term sequelae. Acute irradiation of dogs with 126-510-MeV protons induced a radiation lesion, the severity of which depended essentially on the radiation dosage and, to a considerably lesser extent, on proton energy. A comparison of acute exposure of dogs to divided doses of high-energy protons or x-rays of 180 kV in comparable doses and within the same interval also failed to demonstrate any qualitative differences in severity or time of manifestation of the main symptoms of radiation sickness. Only hemorrhagic signs were more marked under the influence of protons. The coefficients of relative biological effectiveness (RBE) of 126-510-MeV protons constituted 1.0-1.2 for dogs. The increase in RBE with exposure to 510-MeV protons (as compared to small mammals) is related to the larger body dimensions, and particularly to the increased LET from secondary particles within the body [37, 38].

The main research dealing with prevention of radiation lesions in dogs, which are induced by high-energy protons, was conducted by the team headed by V. D. Rogozkin. They studied [8] the efficacy of a protective and therapeutic complex with multiple exposure to 510-MeV protons (3 times a week for 6 weeks, cumulative dose of ~650 rad). The dogs were given cystamine with amygdalin, as well as a complex of other agents--vitamins, serotonin, which is a stimulator of hemopoiesis, prednisone and antibiotics--1 hour before exposing them to radiation. All of the control dogs expired due to acute and severe radiation sickness. About 80% of the animals given

protective and therapeutic agents survived to the 60th day. The clinical signs of lesion in the latter animals were characterized by less severity of hematological and hemorrhagic syndromes. However, it must be noted that the protective and therapeutic combination, which elicited a beneficial effect on early manifestations of radiation damage, did not cause survival of protected dogs at the long term. Six out of seven dogs that survived the acute period died 3.5 months after irradiation due to aplastic anemia. In the opinion of the authors, erythropoietic aplasia could be related to greater damage by protons to nucleic metabolism than in the case of x-radiation. However, it appears to us that the authors did not calculate accurately the time of administration and, perhaps, dosage of blood stimulators and prednisone in their work, which was of an exploratory nature. The possibility cannot be ruled out that administration of blood stimulator and prednisone at the time of irradiation could be associated with stress on the hemopoietic system, and "spurring on" bone marrow depleted by radiation could lead to subsequent aplasia. The opinion that it is dangerous to stimulate hemopoiesis in cases of total-body ionizing irradiation delivered in absolutely lethal doses has also been voiced by other researchers [12, 39-42]. Nevertheless, the above study was of basic significance to the search for means of preventing and treating large mammals exposed to lethal doses of high-energy protons. The results of this same study revealed that use of a virtually analogous protective and therapeutic complex (without serotonin and prednisone) with repeated exposure of dogs to x-rays elicited 50% survival, versus absolute death of control animals.

Studies have also been made of protection of dogs against nonlethal doses, 55-160 rad of 126 MeV protons [43]. The protective efficacy of a vitamin and amino acid complex (amitetravite) containing vitamins C, B₁, P, B₆ and amino acids (tryptophan and histidine) was investigated. Amitetravite was given to dogs by mouth for 2.5-4 weeks prior to irradiation (protective variant) and 2-3 weeks after (protective-therapeutic variant). In addition to amitetravite, some animal groups were given a single dose of amygdalin before irradiation, or additional therapeutic agents after. Amitetravite given before or after irradiation attenuated the manifestations of radiation sickness. With all of the tested doses of radiation, amitetravite attenuated changes in hemopoiesis induced by protons, and in particular it prevented a reduction in number of lymphocytes. The severity of changes in immunobiological reactivity, as well as duration of such changes, were substantially lower in animals given amitetravite than in controls [44]. On the basis of these studies [43, 44], it was concluded that administration of amitetravite prior to exposure to protons in nonlethal doses has no advantages over giving it after exposure (both alone and with other therapeutic agents). The main mechanism of action of amitetravite is enhancement of general nonspecific resistance of the organism, including radioresistance [45].

The complexity and diversity of pathogenetic mechanisms of development of radiation sickness determine the success of complex therapy aimed at different pathogenetic elements [46]. From this point of view, as well as on the basis of the results of studies [47], some variants of therapy were tested on dogs exposed to 275-MeV protons in doses of 250 rad (LD₅₀) and 380 rad (LD₁₀₀). Administration of a group of products (antibiotics, vitamins, hemopoietin, prednisolone, calcium gluconate, bacterial endotoxin) only after irradiation resulted in survival of all dogs exposed to radiation in a dose of 240 rad and 50% of the animals exposed to the minimal absolutely lethal dose (380 rad). It was observed that there is approximately the same therapeutic effect on dogs exposed to acute proton radiation and γ-radiation in comparable doses [48].

In recent years, data have been published on the use of mexamine in dogs exposed to acute lethal radiation from 240-MeV protons [49, 50]. Preventive administration of mexamine to the animals prior to delivery of 400 rad radiation failed to elicit a radioprotective effect. At the same time, a combination of mexamine and shielding of a bone marrow segment at the time of irradiation resulted in 36% survival among the dogs. This was almost 3 times higher than the survival rate among dogs (12.5%) in whom an analogous section of bone marrow was shielded during exposure to protons, but who were not given the radioprotective agent. Thus, the results of these experiments demonstrated that it was possible to obtain an enhanced protective effect in dogs submitted to lethal doses of high-energy protons, when each element of protection (protective agent and shielding of a circumscribed segment of bone marrow) was ineffective when used separately.

As can be seen from the data submitted above, it can be noted that the question of feasibility of chemical protection of animals exposed to the corpuscular radiation of high-energy protons has been answered in the affirmative. The degree of radioprotection of animals exposed to protons differs little from the protection against standard forms of electromagnetic radiation in comparable doses. The same direction of changes in hemopoietic organs, manifested primarily by attenuation of bone marrow cell lesions, was observed in response to giving protective agents before irradiation. A comparison of the radiation effects of electromagnetic radiation and corpuscular radiation from 120-660-MeV protons, as well as of the effects of chemical protection, indicates to some extent that the chief mechanisms of development of the pathological process under the influence of the above-mentioned types of radiation are similar, while the mechanism of radioprotective action of chemical agents is the same with both forms of radiation. This circumstance makes it possible to use models of proton lesions and attenuation thereof in experiments with standard radiation, in particular on dogs. Thus, the way is open for continued search and study of variants of chemical protection and therapy of these animals, not only after single, but long-term irradiation, as they relate to the tasks and objectives of space radiobiology.

Soviet and foreign researchers are working successfully in this direction within the framework of international collaboration on the Interkosmos program [51].

The presence of protective properties in radioprotective agents and combinations thereof, as well as in biological agents with exposure to high-energy protons served as the basis for elaborating measures for pharmacological protection of cosmonauts against corpuscular radiation from solar bursts during missions aboard the Soyuz manned spacecraft [52, 53].

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PHARMACOLOGICAL AGENTS FOR THE PREVENTION AND TREATMENT OF MOTION SICKNESS

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[Text] For a long time now much attention is being given to the study of a state that is characterized by a typical group of symptoms, the appearance of which is related to the use of various forms of transportation. This syndrome has different names: sea and air sickness, kinesis, motion sickness (MS), satellite ["sputnik"] sickness and others.

Many studies have been devoted to the etiopathogenesis of MS [1-7], and they have analyzed the current conceptions of etiology, pathogenesis, mechanisms of onset, symptoms and simulation of MS. The MS problem is quite extensive and is still far from solution. The main questions that must be answered pertain to the substance and biological significance of this state, which cannot be qualified as a pathological process. The MS syndrome is more referable to functional disorders of a reversible nature that have marked symptoms, in which there is prevalence of vegetative reactions that have a substantial influence on man's well-being and fitness. The lack of direct experimental data on the pathogenesis of MS makes it considerably more difficult to work out means of rational pharmacological prevention and treatment of the "seasickness" syndrome.

Research pertaining to man's exploration of space served as an important impetus for the study of pathogenetic mechanisms of MS, as well as the search for new methodological approaches to assessment of vestibular vegetative reactions, formation of conceptions and ideas about MS, and development of preventive and therapeutic agents. Of all the cosmonauts who have participated in space flights, every third one presented varying degrees of MS symptoms, and every fifth one experienced illusory sensations of body position [8].

By now there are many products that have been tested as therapeutic and preventive agents for various forms of seasickness. It is difficult to name a group of drugs that has not been tested for seasickness. However, all of the research work (especially at the earlier stages) was conducted without the use of placebo and a standard; the conditions under which MS developed, group of subjects were not taken into consideration, etc. Quite often, the conclusions concerning the efficacy of drugs were based on a small number of cases [9].

We should like to emphasize in particular that the success of a search for agents against seasickness depends largely on the proper choice of method of study. There are two main approaches to this problem: reproduction of the different, most typical symptoms of MS and reproduction of the entire seasickness syndrome. With the proper choice, both can yield valuable information about the efficacy of drugs, while the first method is also very important to identification of the mechanism of protective action of products and demonstration of mechanisms of development of MS [10].

Methods of quantitative assays of efficacy of agents against seasickness made in slowly revolving systems (SRS) [11, 12] and those based on the otolith reaction of V. I. Voyachek [13] are the most informative, particularly since strict and comprehensive tests on ships and aircraft involve considerable difficulties and are costly.

When testing agents against MS, one should adhere strictly to the following rules [14].

1. First of all, simultaneous testing, not only of a new drug and placebo, but also a standard is a mandatory prerequisite for objective comparisons of different agents, since the standard makes it easier to compare products to one another. At the present time, scopolamine has been adopted as the standard.
2. It is imperative to take into consideration the factor of habituation to motion when making tests on the same object (over a period of several weeks).
3. It is desirable to use the double blind method, with mandatory use of placebo, to eliminate the psychological factor in drug action. Brand and Perry [15] intentionally omitted in their survey studies that were conducted without the use of placebo.

All of the drugs tested for MS can be traditionally, though quite arbitrarily, divided into six main groups: 1) cholinolytics; 2) adrenomimetics; 3) antihistamines; 4) agents that depress the central nervous system (CNS) and tranquilizers; 5) products referable to other pharmacological groups (vitamins, antiemetics and others); 6) combined products.

Cholinolytics: Cholinolytics are among the first products tested for seasickness. This is related, first of all, to the fact that many of the symptoms of MS resemble the effects of stimulation of the parasympathetic nervous system. In this group, belladonna alkaloids--scopolamine, atropine and hyosciamine--have been studied the most extensively.

Many studies have been devoted to scopolamine, and they were conducted both during rolling motion of the most diverse origin and in laboratory experiments involving exposure of man and animals to various levels of accelerations. It is equally effective against MS induced by vestibular, optokinetic or combined vestibulo-optokinetic stimulation [16].

Scopolamine is still one of the most effective agents against MS. Some authors [17] report that scopolamine in a dosage of 0.6-0.8 mg has a protective action for 8 h on 50-60% of the individuals subject to MS. Others believe that the protection index of scopolamine is close to 90% [18, 19]. Analysis of data in the literature, which was made by Wood et al. [20] using a computer, revealed that the protection index for scopolamine is 63%. Doses of 0.6-1.0 mg are considered

to be the most effective, although even small doses, such as 0.1-0.2 mg, have some protective properties [12]. Doubling the recommended dosage does not enhance the pharmacological action of scopolamine, but intensifies its side-effects [17, 21]. More recently, a report was made about the advantages of hypodermic injection of scopolamine (attenuation of side-effects and prolongation of action) [22].

Scopolamine, unlike atropine, has a sedative effect on the CNS. Perhaps its prophylactic effect on MS is related to this, to some extent. There is marked variation of individual sensitivity to scopolamine, and for this reason signs of CNS excitation are occasionally observed after intake thereof, instead of sedation.

With regard to determination of the mechanisms of development of MS, data obtained from studies where seasickness was simulated in man are of some interest; they revealed that the protective action of 1 mg scopolamine is less marked in individuals with arterial hypotension than those with normal arterial pressure [23].

It was proven [24] that the efficacy of atropine, which is a mixture of dextro- and levo-rotatory isomers, is entirely attributable to the presence of one isomer, called hyosciamine.

Hyoscine aminoxide (scopodex) in a dosage of 2 mg was used for a long time on airlines, and it was considered to be the agent with the fewest side-effects. But prolonged intake of scopodex leads to the same undesirable signs as scopolamine; for this reason, Chinn and Smith [25] recommend that it be used in a dose of 1 mg.

Noxiron, an atropine-like substance with marked sedative action, is moderately effective against seasickness [26]. At the same time, amizil [benactyzine], which is a potent central cholinolytic, was found to be an ineffective agent when tested in SRS.

It was established that central cholinolytics, which block central cholinergic structures, have a therapeutic effect on parkinsonism. This made it necessary to search for new synthetic analogues of belladonna that would have a more selective cholinolytic action. However, most of the products used to treat parkinsonism were found to be ineffective for MS [26, 27].

Analysis of data in the literature indicates that none of the cholinolytics that cannot penetrate the hematoencephalic barrier prevents MS. Moreover, scopolamine loses its protective properties if the tertiary nitrogen in its molecule is replaced with a quaternary (buxopan). This indicates that blocking of central cholinergic synapses is significant in the mechanism of protective action. The opinion is held [16] that synapses of the vestibular nuclear complex may be the most probable region of primary action of this group of MS drugs. This conclusion is based on the decline in "resting" discharge of the nerve and absence of neuronal reaction to rotation, which were observed in experiments on cats after irrigating these nuclei with belladonna alkaloids [28] or dimenhydrinate [29].

Adrenomimetics: Of the entire group of products that affect adrenergic structures, apparently only sympathomimetic amines with marked central stimulating action (ephedrine, phenamine and others) are of interest with regard to finding drugs against seasickness.

Products with adrenolytic properties (phenoxybenzamine and others) not only fail to diminish sensitivity to vestibular stimuli, but can produce the main symptoms of MS [17].

As far back as 1937, Hill [30] observed the preventive value of the adrenergic agent, benzedrine (phenamine, amphetamine). Its beneficial effect on MS was discovered by chance when phenamine was given against the drowsiness induced by scopolamine. According to the data of Albrecht [31], phenamine was effective against seasickness aboard vessels, but did not have an effect during flights. Subsequently, the efficacy of phenamine was demonstrated by a number of authors in simulating MS under laboratory conditions [13, 21, 32]. It was established [17] that benzedrine in a dosage of 10 mg is close in efficacy to antihistamines when used in SRS. When the dosage was increased to 20 mg, its action increased even more; however, this was also associated with significant increase in side-effects.

The studies of V. A. Golovko et al. [33] revealed that phenamine given to prevent seasickness also increases statokinetic stability. The authors believe that phenamine, which increases excitability of the ascending activating system of the reticular formation, changes self-regulation of functional systems of the body to a different, higher level of self-regulation.

Use of ephedrine as an agent against seasickness revealed that it was moderately effective on water [34] and ineffective for air sickness [23]. A. P. Yaroslavskiy [35] observed intensification of vestibulovegetative reactions after intake of ephedrine. Wood and Graybiel [17] demonstrated moderate efficacy of 50 mg ephedrine (the same as with phenamine in a dosage of 10 mg) in studies in SRS.

In our opinion, the differences in effects of sympathomimetics on the sea and air forms of motion sickness are related to their predominantly stimulating influence on peripheral adreno-reactive structures, which increase statokinetic stability.

With regard to the search for products against MS, sympathomimetics with central stimulating action are interesting in that they can be used in combination with other agents to remove the depressing influence of other, more effective agents (cholinolytics, antihistamines) against MS.

Antihistamines: Most antihistamines not only depress the effect of histamine on body functions, but actively affect cholinoreactive and adreno-reactive systems. In this class of compounds, which numbers several thousand products, many agents have been found that have protective properties against MS.

In 1949, the report of Gay and Carliner was published [36], concerning the high activity of dimenhydrinate (dramamine) in the presence of seasickness. Subsequently, the efficacy of dimenhydrinate was confirmed with other forms of motion sickness [37-39]. In studies with SRS, dimenhydrinate in a dosage of 50 mg was one-third as active as scopolamine [17]. Analogous results (as compared to scopolamine) were obtained under the influence of optovestibular and optokinetic Coriolis effects [16].

Dimedrol (diphenylhydramine, benadryl) is also one of the recognized agents against MS in different environments. In a dosage of 50 mg, its efficacy is comparable to that of dramamine, and it constitutes about 60% [20, 40, 41].

Later on, other agents were found in this group of antihistamines that were active against MS. This applies, first of all, to cyclizine or marezine. According to the data of Trumbull et al. [28], this product in a dosage of 50 mg prevents seasickness in 100% of the cases. Lederer and Kidera [42] reported on the analogous

efficacy of cyclizine during flights aboard passenger aircraft. Brand et al. [43] demonstrated a preventive effect already after intake of 15 mg cyclizine. The authors believe that the efficacy of 50 mg cyclizine equals that of 0.1 mg scopolamine. According to M. I. Nikol'skaya [13, 32], cyclizine in a dosage of 50 mg was just as effective as 1 mg scopolamine when used in the Voyachek otolith test. Wood et al. [20] believe that the protection index of cyclizine is 71%. However, in more recent studies conducted in SRS considerably less activity was demonstrated for this product.

It must be noted that cyclizine has a mild side-effect and strong therapeutic effect [44]. On this basis, cyclizine was included in the onboard medicine kits of the Mercury, Gemini and Apollo spacecraft as a means of preventing MS. The drawback of this product is that it is brief acting.

Chlorcyclizine (perazil) prevents seasickness to a lesser degree than cyclizine [45].

Meclizine (navicalm, bonamine) differs advantageously from other products in that it has a longer effect. A dose of 50 mg taken 24 h before taking a flight provides protection against air sickness [48]. In studies conducted on vessels, this product was given once a day; however, it was just as effective as others taken three times a day [25, 47, 48]. The protection index is 50-85%. However, in the presence of "severe rolling" on artificial waves, meclizine had no protective effect [44]. Studies in SRS using this product in doses of 50 and 150 mg also yielded a rather questionable effect [17].

Cinnarizine also has a long action, but its effect is not constant [27]. It was shown that, in a dosage of 50 mg, cinnarizine prevents development of MS in an SRS; however, it is entirely ineffective against air sickness [17, 49]. Single intake of this product by mouth in a dosage of 250 mg had an effect similar to that of meclizine, but 50% of the subjects presented drowsiness [50].

Antihistamines of the phenothiazine group have marked sedative activity. Of this group of antihistamines, diprazine (promethazine, pipolphen, phenergan) has been studied the most in relation to MS. Glaser and Hervey [19] believe that diprazine is more effective than dimedrol. Use of diprazine 3 times a day in a dosage of 25 mg when transporting troops on water was effective in 70-78% of the cases.

Of considerable interest are studies of recently synthesized selenium-containing derivatives of ethylene diamine, which are active for 3 days [51].

The mechanism of protective action of antihistamines is utterly unknown; there is no parallel between antihistamine activity and capacity to prevent seasickness. The most active antihistamines, such as pheniramine, chlorpheniramine, neo-antergan and others are not effective against MS. It must be noted that they expressly are characterized by an excitatory effect on the CNS [52].

At the same time, cyclizine and meclizine, which are effective against seasickness, are referable to the mildest antihistamine compounds.

It may be considered that the attenuation of MS symptoms by antihistamine agents is most likely attributable to their anticholinergic, rather than peripheral antihistamine activity [53, 54]. Moreover, many of them have a sedative effect and can prevent vomiting.

Agents that depress the CNS and tranquilizers: Noble [55] demonstrated that many barbiturates (sodium pentobarbital, phenobarbital, veronal and others) can prevent seasickness in dogs. However, in experiments involving man only barbitals were effective. No parallel was found between the hypnotic effect and capacity to prevent seasickness.

A. I. Vozhzhova [56] discovered that barbitals had a substantial effect on dogs with artificially induced seasickness. He prevented vomiting entirely in 53 out of 59 dogs. Preventive intake of barbitals in a dosage of 1g 1 h before "rolling" prevented MS in 70% of the cases. There is 2-3-fold decline in efficacy of this product when given for therapeutic purposes, i.e., when there is already manifestation of the seasickness syndrome [57].

Rauwolfia products (reserpine, ameroxilon) were ineffective against seasickness [58]. There was even an increase in incidence of vomiting at sea after intake of 0.3 mg reserpine.

In the tranquilizer group, meprobamate (meproten, andaxin) was found to be effective; in a dosage of 400 mg it had a protective effect against air sickness in 60% of the cases [59].

Neuroleptics of the phenothiazine class may be of special interest, since they have a marked antiemetic action.

Aminazine (chlorpromazine) is the best known representative of this group. This product has adrenolytic and mild antihistamine activity; it has a strong sedative and antiemetic action. It controls vomiting induced by apomorphine or resulting from some pathological process.

R. A. Okunev [60] demonstrated that the efficacy of aminazine in a dosage of 50 mg constitutes 87% for seasickness. However, the results of more comprehensive studies revealed that this product does not have a protective effect against various forms of motion sickness [40, 58].

Addition of a piperazine ring into the structure of this product enhances sedative and antiemetic activity. Thus, prochlorperazine (compazine, stemetil) is 4 times more active as an antiemetic than aminazine. According to the data of Wheeler et al. [61], this product prevented nausea and vomiting when given in doses of 10 and 15 mg in 84% of the cases of seasickness. Intake of prochlorperazine was also effective against air sickness [49, 62]. M. I. Nikol'skaya [32], who conducted studies using the otolith test, established that prochlorperazine in a dosage of 10 mg is as effective as scopolamine. However, its protective action was not demonstrable in an SRS [17, 21].

Denson [63], who conducted experiments with 12 rotating subjects, failed to demonstrate changes in vestibular reactions (nystagmus, cupulograms, subjective estimation of angular displacement) after intake of prochlorperazine in a dosage of 10 mg. This led him to assume that the action of this product does not affect central connections of the vestibular system.

Ethaperazine (perphenazine) has been studied rather extensively in relation to seasickness; it is about 20 times more active as an antiemetic than aminazine [64]. It was ineffective against sea and air sickness, as well as in the otolith test

of Voyachek [44, 65, 66]. There are indications [67] of efficacy of thiethylperazine (torecan) in 78% of the cases of seasickness. An analogous effect was demonstrated against air sickness [68]. Intake of torecan for treatment of vertigo of diverse etiology (Meniere's disease, labyrinthopathy of diverse etiology and others) elicited a good therapeutic response in 60-70% of the cases [69, 70]. Experiments in SMS revealed that torecan in a dosage of 10 mg does not increase resistance to seasickness, whereas in a dosage of 30 mg it even diminishes it [21]. This product is interesting because it is selectively localized in the cerebellum and nucleus fastigii [70].

We need more definition of data pertaining to the efficacy (70-80%) of triftazin (stelazine, trifluoperazine) against seasickness, since there was no control in studies thereof [73, 74].

In recent years, some products have been developed that are referable to the phenothiazine class, whose sedative and antiemetic effects are considerably greater than those of aminazin. Perhaps, there may be highly effective agents against MS among these products.

Products referable to other pharmacological groups: In the search for agents against seasickness, vitamins were also tested. Although these products have some beneficial effect on vomiting of diverse origin, they have minimal efficacy. In 1953, Benkendorf [73] reported on the successful treatment of seasickness with pyridoxine. More comprehensive testing at sea revealed that vitamin B₆ is ineffective [58]. In the same studies it was established that thiamin, nicotinamide and calcium pantethonate have no protective effect against MS.

The data obtained by Yu. F. Udalov et al. [74] indicate that a pyridoxine deficiency could be the cause of diminished vestibular stability. On this basis, the authors proposed pyridoxal hydrochloride and ATP as an agent against motion sickness [75, 76].

According to the data of N. L. Suslova et al. [77], amitetravit, which consists of vitamins B₁, B₆, C, P and amino acids (tryptophan and histidine) increases vestibular stability negligibly after intake for 2 weeks.

Intravenous or rectal administration of sodium bicarbonate has a preventive and therapeutic effect on MS. This finding was first made on rabbits by Hasegawa [78]. Subsequently, he also demonstrated the efficacy of sodium bicarbonate in man with regard to seasickness [79].

In the USSR, the method of using sodium bicarbonate against MS was developed by V. N. Barnatskiy [80, 81].

The assumption has been voiced that there is an extralabyrinthine mechanism of action in sodium bicarbonate, which is based on changes in metabolic processes and the mediated effect of this product on cardiovascular, respiratory and renal activity. This was confirmed to some degree by the studies of G. I. Gorgiladze and B. B. Yegorov [82], who demonstrated that neither single nor multiple intravenous injections of sodium bicarbonate altered otolith reactions.

There have been reports of efficacy of diphenidol (an antiemetic) for seasickness, under laboratory conditions and with damage to the labyrinth [83, 84].

Testing of local anesthetics (cocaine, anesthesin) on water [60] and in the air [85] showed them to be minimally effective. Spasmolytic products, such as amyl nitrite, nitroglycerin and papaverine, were also found to be ineffective.

G. L. Komendantov and N. A. Razsolov [86], who studied the distinctions of stress states in pilots by the method of double rotation, found that intake of the Vzletnaya ["take-off"] caramel delayed by 3.17 times the time of occurrence of MS.

Combined products: The principle of combining drugs has been long since used in pharmacology to eliminate the undesirable effects of the main product or products. The advantage is, first of all, that by combining the most effective agents against MS one can summate or even enhance their effects.

Not infrequently, there are not sufficient theoretical grounds for the combined or successive use of drugs, or else there is no preliminary pharmacological study of their interaction. For this reason, when developing complex formulas, one must know the pharmacodynamics of each constituent and take into consideration a number of other factors, such as physicochemical, pharmacokinetic, metabolic, individual compatibility, etc. The studies of A. I. Vozzhova [56] can serve as an example; she demonstrated that a beneficial response was noted in only 47% of the cases when barbitol was washed down with water. If, however, it is washed down with an 0.5% solution of citric acid, the efficacy rises to 77%.

For a long time, it was not possible to find a combination of products that would be more effective than scopolamine. The chief advantage of combined products is that they are better tolerated and there are fewer undesirable manifestations.

Aeron, which is a mixture of camphorates of scopolamine and hyoscyamine (0.1 and 0.4 mg, respectively), is a well-known product. However, one would think that the protective action of aeron is entirely attributable to scopolamine, since it has been demonstrated that hyoscyamine does not elicit a good response, even after intake in a dosage of 0.7 mg [15]. The low efficacy of aeron is attributable to the low scopolamine content.

The efficacy of "NII tablets," which are a combination of scopolamine camphorate, hyoscine and nicotinic acid [87], has been tested.

N. Ya. Lukomskaya and M. I. Nikol'skaya [10] tested 5 combinations of drugs, the chief constituent of which was scopolamine in a dosage of 1 mg. Using scopolamine in combination with antihistamines, the authors expected to find a combination that would yield summation of the main effect (mixture No 2: 1 mg scopolamine + 10 mg stemetil; mixture No 3: 1 mg scopolamine + 50 mg cyclizine). They used phenamine to eliminate central side-effects (mixture No 4: mixture No 3 + 5 mg phenamine; mixture No 1: mixture No 3 + 10 mg phenamine) and proserine [neostigmine] to eliminate peripheral side-effects (mixture No 5: mixture No 4 + 10 mg proserine).

Evaluation of the protective action of the tested drugs according to the mean number of otolith tests tolerated revealed that mixtures containing scopolamine and cyclizine (mixtures Nos 1, 3, 4 and 5) were highly effective. They were 1.5 times more effective than 1 mg scopolamine. It must be noted that addition of phenamine did not enhance the protective effect, although phenamine by itself does have some efficacy. Addition to the mixture of proserine reduces several undesirable effects, in particular, dryness of the mucous membranes.

A. I. Vozzhova and R. A. Okunev [88] reported on the high efficacy of mixtures of aminazin (50 mg) with caffeine (200 mg) and dimedrol (50 mg), as well as diphasin (50 mg) with caffeine (200 mg) and dimedrol (50 mg) against experimental seasickness.

P. I. Syabro [89-91] proposed several complex products (platybrin, plaviphen, pheplavin) on the basis of conceptions of seasickness as a reflex reaction. Trials of these mixtures on 306 airline passengers confirmed their high efficacy [92].

In recent years, American scientists reported the high efficacy of combinations of scopolamine with d-amphetamine (benzedrine) and promethazine with ephedrine, which made it possible to include these drugs in the medicine chests for the crews of the Skylab orbital station (OS) [93].

The high efficacy of the first combination (scopolamine + d-amphetamine) was discovered by chance, when amphetamine was given against drowsiness due to scopolamine bromhydrate [49]. The best result was obtained with intake of 1.2 mg scopolamine combined with 20 mg d-amphetamine; however, this prescription cannot be used on a broad scale, since there are marked side-effects. A combination of 0.6 mg scopolamine and 5 mg d-amphetamine (lomotil) must be considered the best. The cosmonauts aboard the Skylab OS took a product consisting of 0.35 mg l-scopolamine and 5 mg d-amphetamine (lomotil) against MS. However, combining scopolamine with d-amphetamine, as well as lowering the dosage of scopolamine, cannot eliminate entirely the undesirable effects [94].

Combinations of scopolamine (0.6 mg) with other sympathomimetics--ephedrine (50 mg)--have a strong protective effect [17]. High protective activity has also been demonstrated in a combination of antihistamines--promethazine (diprasin, pipolphen)--and ephedrine (25 mg each) in tests under both experimental [95] and operational conditions [49]. This combination, in the opinion of the authors, raises the thresholds of stimulation, lowers MS reactions and is effective against all forms of motion. Johnson et al. [96] believe that, although the efficacy of a combination of promethazine hydrochloride (25 mg) and ephedrine sulfate (25 mg) is the same as that of a combination of l-scopolamine hydrobromide (0.35 mg) and d-amphetamine sulfate (5 mg), it is best to use promethazine with ephedrine for treatment of MS.

A mixture of another antihistamine, dimenhydrate (50 mg) with ephedrine (50 mg) was also found to be moderately effective. A reduction of ephedrine dosage to 25 mg diminished the protective effect.

It must be noted that the effect of antihistamines, in particular meclizine, is not enhanced when given in combination with d-amphetamine [17].

The syndrome that is known among specialists in the field of space and aviation medicine as MS is usually manifested within the first 5-7 days of a flight. Its onset is related to changes in functional state of the vestibular analyzer, impaired interaction of afferent systems, hemodynamic distinctions, etc. In spite of the relatively rapid adaptation to weightlessness, the manifestations of MS have a considerable effect on the efficiency of crews during the important stages of an orbital flight.

The problem of preventing MS acquired even more importance in connection with the increased role of man in controlling the flights and landings of reusable spacecraft.

Graybiel, a prominent American specialist in this field, believes that in searching for ways and means of preventing MS one should concentrate chiefly on pharmacological products. In spite of all the complexity of this problem, we need a drug that would not only prevent MS, but would have no side-effects that would influence man's fitness. The foregoing defines the requirements for drugs to prevent and treat MS.

To date, a number of products and combinations thereof have been proposed as agents for the prevention and treatment of MS. However, all of them are far from meeting in full the requirements made of them. For this reason, the search for effective drugs for prophylaxis and therapy of MS remains as a pressing task to this day. Attention should be concentrated on methodology and informativeness of methods used for quantitative evaluation of the efficacy of drugs in experiments on animals and studies involving man.

There is no question that successful development of effective agents for the prevention and treatment of seasickness is only possible by means of wise combinations of drugs referable to different classes of chemical compounds. In our opinion, one should abandon the search of preventive agents among narcotics and tranquilizers. Dopaminergic substances, metabolites and antimetabolites merit special attention, since a set of physiological and biochemical factors plays the leading role in the pathogenesis of MS, and their essence must be identified. Development of such a product will constitute a definite contribution to public health care in general and space medicine in particular.

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EXPERIMENTAL AND GENERAL THEORETICAL RESEARCH

UDC: 629.78:[612.881+612.886

RESULTS OF STUDIES OF VESTIBULAR FUNCTION AND SPATIAL PERCEPTION IN THE CREWS OF THE FIRST AND SECOND EXPEDITIONS ABOARD SALYUT-6 STATION

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[Article by I. Ya. Yakovleva, L. N. Kornilova, G. D. Syrykh, I. K. Tarasov and V. N. Alekseyev, submitted 31 Jan 80]

[English abstract from source] The results of studies of the vestibular function and spatial perception function in the crew members of long-term (96- and 140-day) space missions aboard Salyut-6 are presented. Similar changes and individual variations are revealed. All the cosmonauts have shown the following changes: increased reactivity of the otolith organ, decreased sensitivity of the cupular system, asymmetry of most parameters studied and illusory reactions in flight. Individual reactions are as follows: level of changes, dynamics and time of recovery, development of vestibulo-vegetative symptomocomplex during early adaptation to zero-g, signs of decline in vestibulo-vegetative tolerance post-flight and changes in reciprocal relations between the otolith organ and semicircular canals.

[Text] It is known that vestibulovegetative disorders and impaired spatial perception occurred among most cosmonauts in flight. They were the most marked during the period of initial adaptation to weightlessness and early stage of readaptation to earth's conditions.

Many opinions and hypotheses have been expounded concerning the genesis of these disturbances. Leading significance is attributed to the unusual functioning of the vestibular system and systems that interact with it [1-3].

Isolated works have been published about human vestibular function during long-term weightlessness, and their results are contradictory [2-5].

Our objective here was to define vestibular reactions and spatial perception under the combined effect of flight factors and during the readaptation period.

Methods

We evaluated otolith function by means of an advancing visual image, according to size of the angle of counterrotation of the eyeball when moving from vertical to

horizontal position (on right and left side), which is a modification of the method of indirect otolithometry of Fischer and Fluor [6, 7].

We evaluated the function of the semicircular canals according to magnitude of thresholds of sensitivity to changes in angular velocity (according to nystagmus and sensory component). The sensations of change in angular velocity were determined with a constant angular acceleration of $1^\circ/\text{s}^2$.

We examined the distinctions of interaction between the otolith system and semicircular canals (according to nystagmus and sensory component) by means of the "otolith reaction" test of Voyachek (OR).

Perception of spatial coordinates (gravitational vertical and horizontal) was examined using the Vertikal' [vertical] instrument in "seated" position and in horizontal position, on the right and left side.

Vestibulovegetative stability was evaluated according to endurance of the cumulative effects of Coriolis and precession accelerations using the Bryanov method [8], as well as the cumulative effect of rectilinear accelerations on the 4-pole swing of K. L. Khilov, graded optokinetic stimulation with the subject moving to an unstable support and exposure to angular accelerations (modified Barany test).

Determination of level of vestibular stability was associated with registration of a broad set of clinical and physiological parameters (arterial pressure by the tachoscillographic method, pulse from the electrocardiogram, cardiointervalography, intensity of vegetative reactions according to K. L. Khilov, electronystagmography and others).

We tested otolith function, semicircular canal function and perception of spatial coordinates 3 to 6 times in the background study (30-45 days before the flights) and as many times on the 1st-2d, 3th-5th, 8th-9th days and 1st-2d months after them.

The level of vestibulovegetative stability was tested thoroughly 60-45 days before the flight, 3-5 days before liftoff, on the 4th-5th and 8th-9th postflight days according to endurance of the Barany test and OR.

These studies were conducted on members of the crews of the first (96-day) and second (140-day) expeditions aboard Salyut-6.

Results and Discussion

In the background tests, the indicator of otolith function did not exceed the range of physiological fluctuations and constituted $5-12^\circ$ in all of the cosmonauts. In all of them, with the exception of the commander of the first expedition, the otolith reflex was symmetrical, or else asymmetry ($2-3^\circ$) did not exceed the range of physiological scatter (3°). In the commander [CDR] of the first expedition, asymmetry exceeded the physiological scatter (2° on the right side and 10° on the left).

The base thresholds of sensitivity to changes in angular velocity were in the physiological range of this parameter ($2-6^\circ/\text{s}$), as determined in a mass survey of healthy individuals with vestibular stability, constituting $4-6^\circ/\text{s}$ in all cosmonauts with the exception of the CDR. The thresholds to acceleration and slowing

were virtually the same, and asymmetry did not exceed $2^{\circ}/s$. In the CDR of the first expedition, the threshold of sensitivity to a change in angular velocity was elevated ($11^{\circ}/s$), and asymmetry constituted $6^{\circ}/s$.

The parameters of accuracy of perception of spatial coordinates were in the physiological range of fluctuations in all crew members ($0-1^{\circ}$ for vertical position, $18:5^{\circ}$ for horizontal lateral) with the exception of the FLE [flight engineer] of the first expedition. The difference in error of perception of spatial coordinates in lateral positions was either absent or in the range of physiological asymmetry (up to 5°).

Studies of interaction between the otolith system and semicircular canals revealed reciprocal relations between them (30-35% decrease in intensity of vestibulosomatic and vestibul sensory reactions of semicircular canals) in all but the FLE of the first expedition. In the latter, there was no inhibition of reactions of semicircular canals after rotation upon bending the head.

At the time of the preflight examination, all of the cosmonauts presented high parameters of vestibulovegetative stability as a result of regular vestibular training that was conducted on an individual basis as part of the preparations. At the time of primary screening, three out of four cosmonauts presented a mean level of vestibular stability in the vestibulometric examination, since they presented moderate and average vegetative reactions at the end of the study.

At the time of primary screening and throughout the training stage, the CDR of the first expedition presented a high level of vestibulovegetative stability. The cosmonauts of both expeditions experienced illusory reactions of the inversion type on the 1st postflight day; in the FLE of the second expedition, this reaction appeared 2 h after the transition to weightlessness, and in the others it occurred immediately after the start of weightlessness. It was possible to suppress the illusion in two cosmonauts by means of fixing on some object, immobilization in the seat, as well as self-training. The illusion that occurred initially lasted for a few minutes to 4 h. Thereafter, the illusion recurred sporadically throughout the mission, most often at times of intensification of motor activity or in the presence of optokinetic stimuli. A sensation of "blood rushing" to the head was experienced by the cosmonauts 1.5-2 h after transfer to weightlessness and was marked for 5-7 days. For the first 3 days, both CDR's and the FLE of the first expedition reported vestibular discomfort when moving the head, manifested by vertigo and mild nausea. The adaptation period was characterized by violent but brief (3 days) reactions in the CDR of the first expedition. There were less marked reactions, but they persisted for a long time during the adaptation period in the FLE of the first expedition. The adaptation period was brief for the FLE of the second expedition, and his reactions were the least marked. The CDR of the second expedition again experienced mild vestibular discomfort upon increasing motor activity (turning, head and trunk movements) 10 days prior to the end of the mission.

For the first few postflight days, the cosmonauts presented statokinetic disorders in the form of instability in Romberg's position and shaky gait, while both CDR's presented, in addition to statokinetic disorders, marked vestibulovegetative ones: vertigo, nausea, retching, which were particularly intensive when moving the head and changing to vertical position.

On the 1st and 2d postflight days, there was bilateral (crew of second expedition) or unilateral (crew of first expedition) hyperreflexia of the otolith reflex of counterrotation of the eyeball (Figure 1). There was greater accentuation of the otolith reflex in the crew of the second expedition (3-5 times more intensive than in the background study).

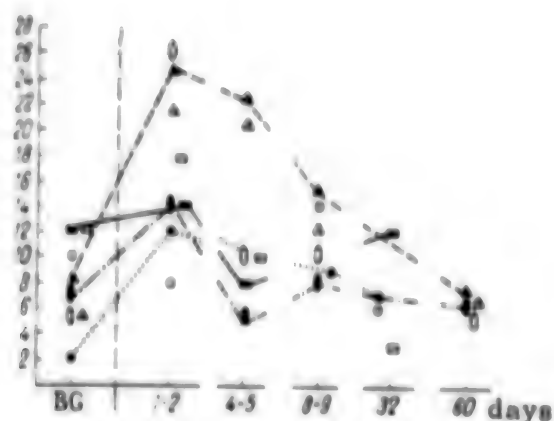


Figure 1.

Dynamics of postflight otolith reflex. Here and in Figures 2 and 3, the circles and hexagons refer to the CDR of the first and second expeditions, respectively; the rectangles and triangles refer to the FLE of the first and second expeditions.

Y-axis, angle of counterrotation of the eyes (degrees); x-axis, day of examination.

Here and in Figure 3, the black symbols correspond to parameters in horizontal position on the right side and white ones, on left side.

Key [here and Figures 2 and 3]:

BG) background

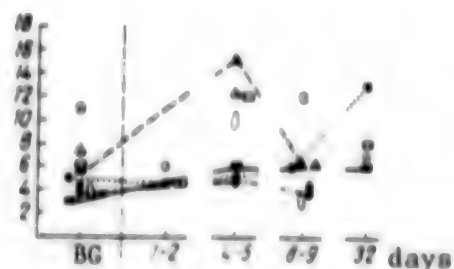


Figure 2.

Dynamics of threshold sensitivity of semi-circular canals to changes in angular velocity after the flight.

Y-axis, angular velocity, °/s. Black symbols refer to acceleration and white to deceleration

After the flight, the cosmonauts presented asymmetry of the otolith reflex, which was characterized by accentuation (by 4-8°) of the reflex when lying on the right side in the CDR of the first expedition and both FLE's, and by hyperreflexia of 12° in horizontal position on the left side in the CDR of the second expedition. During this period, all of the cosmonauts complained of statokinetic disorders, which were confirmed on the subsequent days by objective stabilographic examinations.

Examination on the 4th day revealed a tendency toward normalization of the otolith reflex and decrease in asymmetry in all cosmonauts, with the exception of the FLE of the second expedition. Normalization of otolith function occurred on the 9th postflight day in the CDR of the second expedition, and after 1 month in the CDR of the first one. Asymmetry of the otolithic reflex, the direction of which was the same as on the first few postflight days, reappeared on the 32d postflight day in the FLE of the first expedition.

There was slower restoration of otolith function in the FLE of the second expedition: there was no tendency toward normalization of the reaction on the 5th and 9th postflight days, and it is only in the test 2 months later that the otolith reflex corresponded to background values.

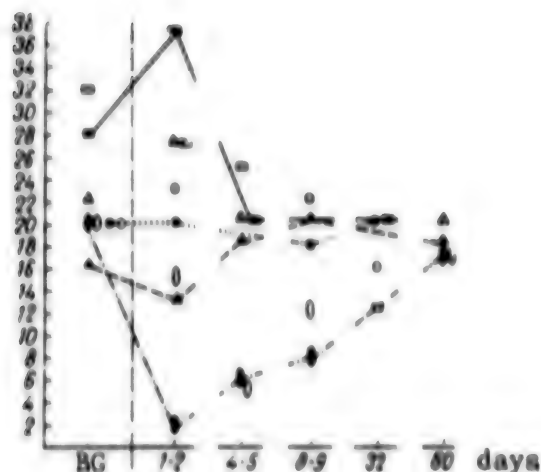


Figure 3.

Dynamics of parameters of accuracy of perception of spatial coordinates in horizontal position on the side, after the flights. Y-axis, perception error (°)

Otolith system and semicircular canals after the flights revealed reciprocity in all cosmonauts, with the exception of the FLE of the second expedition. He did not have an inhibitory otolith reaction to nystagmic and illusory reactions of the semicircular canals.

Examination of perception revealed sensory changes in all cosmonauts (Figure 3), which were characterized by development of substantial asymmetry of error (from 11 to 13°) of perception of the gravity vertical in lateral position in three cosmonauts and change in its direction in the crew of the first expedition (as compared to asymmetry observed before the flight). The error increased to 3° (versus 0.5-1° in the background period) in the CDR of the second expedition in seated position.

Vestibulovegetative stability, which had been high in all cosmonauts before the flight, diminished in the FLE of the second expedition: he presented grade I vestibulovegetative reactions in the Barany test and OR (dryness of the mouth, frequent swallowing movements, pallor of the integument, faster heart rate).

Thus, the results of these studies are indicative of changes in sensory systems and, in particular, in functional state of the vestibular analyzer under the influence of space flight factors.

The following changes were demonstrable to some degree or other in all (or in 3 out of 4) cosmonauts involved in both expeditions: increased reactivity of the otolith system; diminished sensitivity of the cupular system; asymmetry of most tested parameters (otolith reflex, threshold sensitivity of canals, accuracy of perception of spatial coordinates); development of in-flight illusory reactions.

We should refer to the individual distinctions of reactions the degree of changes, dynamics and duration of readaptation period, development of the vestibulovegetative set of symptoms at the early stage of adaptation to weightlessness and readaptation to earth, signs of diminished postflight vestibulovegetative stability, change in nature of interaction between the otolith system and semicircular canals after the flights.

Testing of sensitivity to changes in angular velocity (Figure 2) revealed that there was brief postflight elevation thereof in the crew of the second expedition, particularly the FLE (from 5° to 15°/s), and asymmetry increased to 5°/s.

There was virtually no change on the first few postflight days in thresholds of perception of changes in angular velocity in the crew of the first expedition. However, when examined on the 5th and 8th days, there was significant (6°) asymmetry of threshold sensitivity to changes in angular velocity, and it persisted in the CDR for 1 month after the flight.

Studies of correlations between the

Our studies did not enable us to demonstrate a correlation between the changes resulting from the flights and initial level of vestibulovegetative stability. This could be attributable to the small number of our subjects.

The results of studies of vestibular function in crew members following long-term space missions, the data referable to the previous 7- and 30-day flights [9, 10], as well as model experiments [11, 12], do not enable us to voice an opinion with any certainty as to the specific mechanism of the demonstrated changes.

We can only assume that a set of factors played some role: impairment of systemic nature of analyzer function, dynamic changes in blood and spinal fluid, as well as general change in regulatory influences during space flights.

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RESULTS OF VECTORCARDIOGRAPHIC EXAMINATIONS DURING AND AFTER LONG-TERM SPACE FLIGHTS
ABOARD THE SALYUT-6--SOYUZ ORBITAL COMPLEX

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
pp 23-26

[Article by Z. A. Golubchikova, A. D. Yegorov and V. V. Kalinichenko, submitted
29 Oct 79]

[English abstract from source] In long-term space flights cardiac bioelectric activity was measured by vector-electrocardiography using ECG in 12 standard leads. Most marked changes in the form of a decrease in the integral spatial repolarization vector were seen postflight. This parameter did not return to normal during one month postflight. Depolarization vector and vector orientation remained essentially unchanged.

[Text] Bioelectrical activity of the myocardium was examined during and after 96- and 140-day flights, both to assess the ongoing health status of cosmonauts and to demonstrate general patterns and mechanisms of changes in bioelectrical activity of the myocardium in the course of prolonged weightlessness. For this purpose, we recorded the EKG with subsequent analysis of the dynamics of magnitude and direction of electromotive forces of the heart during and after flights.

Methods

Polynom-2M equipment was used to record the EKG in the 12 standard leads during the flights, with telemetric transmission to earth, and Mingograph equipment was used for the same purpose before and after the flights. Electrodes were applied to the extremities by means of rubber cuffs, while a band was used for the chest electrodes.

In interpreting the EKG, determination was made of the conventional parameters, and for vector analysis we examined leads I and II, V_2 and V_6 (only before and after the flights) and duration of waves in the WRS complex and T.

We used the method of Lamb [1], which was modified to apply to the objectives of our study [2], to make a spatial vector analysis. According to this method, calculation was made of the angle of deflection of the projection of the spatial vector on the horizontal plane from the X axis (angle H) according to the orthogonal precordial leads V_2 and V_6 [3-5]. Coordinates Y and Z of integral vectors of depolarization and repolarization of ventricular myocardium were calculated on the basis of the values of this angle and coordinate X in lead I.

The principle of spatial quantitative analysis is warranted by the fact that we had to evaluate the dynamics of magnitude and direction of vectors, rather than their absolute values, which were affected by local factors, constitutional distinctions and other factors.

We evaluated the following parameters: magnitude of integral depolarization and repolarization vectors ($\overline{MQRS}$ and $\overline{MT}$); angles determining the position of vector projections in the frontal (α) and horizontal (β) planes and deviation of spatial vectors from their projections on the horizontal plane (elevation, γ). In addition, we determined the divergence between integral depolarization and repolarization vectors (θ in space; β in the frontal plane) and vector ratio $\overline{MQRS}'/\overline{MT}$.

Vector analysis of the EKG recorded during the flights was made only in the frontal plane (we determined the magnitudes of vector projections on this plane, $\overline{MQRS}$ and $\overline{MT}$, and the angles describing their position), since we recorded bipolar CR leads under these conditions. In view of the fact that the frequency characteristics of the equipment used in flight and in the ground-based studies were not the same, we did not compare the vector parameters in flight to preflight data, and we considered only the dynamics of these parameters in the course of the flight.

Examinations were made 4-6 times before the flight, 3-4 times during the flight and 5-7 times over the first postflight month. We submit below the findings referable to the first and second crews.

Results and Discussion

There were no appreciable deviations from normal on the preflight EKG of cosmonauts of both crews. Throughout the flights, their heart rate was sinusoidal, and sinus arrhythmia was noted in some tests in all cosmonauts with the exception of the flight engineer of the second crew (FLE-2). The time parameters of the EKG during and after the flight did not exceed the physiological range, and in essence they corresponded to the preflight fluctuations. The shape of the EKG during and after the flight usually failed to reveal any appreciable changes. However, in lead III the T wave became mildly negative on the 5th postflight day in the commander of the first crew (CDR-1) (before and during the flight it had been mildly positive or isoelectric). The ratio of projections of vectors of depolarization and repolarization of ventricular myocardium, as well as their position on the frontal plane, changed in all cases. In view of deviations in operation of the calibrator during some of the examinations, we did not determine the magnitude of in-flight vectors.

In the postflight period, the most consistent change was a decrease in integral repolarization vector. On the day of the landing, this parameter was markedly diminished in all cosmonauts (Figure 1). Subsequently, it increased, but it did not reach the mean preflight level in 3 cosmonauts over a 1-month period. At the same time, in CDR-1, vector MT increased significantly, already on the 1st postflight day, and it exceeded the top preflight level.

Evidently, the decrease of integral vector MT in the postflight period is related to developing signs of vegetative imbalance and, perhaps, it reflects the presence of metabolic changes in the myocardium. After long-term exposure to weightlessness, earth's gravity is a rather potent stimulus that elicits a drastic increase (as compared to weightlessness) in flow of afferent impulsation from mechanoreceptors, which activates the adrenergic system. As a result, there is development of an

unbalanced correlation between tonus of sympathetic and parasympathetic systems, against the background of a strong stressor influence at the descent phase and asthenization due to the long-term flight. Adrenergic influences against the background of prior stress or asthenization induce, as was observed under hypokinetic conditions, a decline in voltage of T waves and, consequently, a reduction of vector T [6].

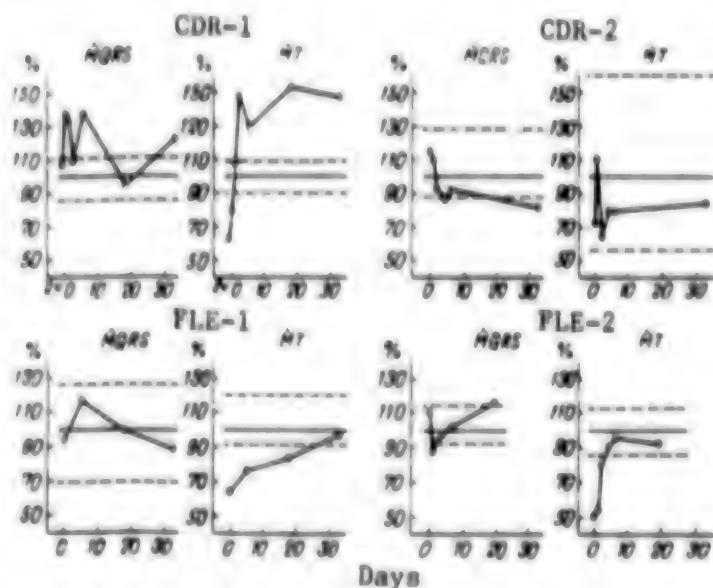


Figure 1.
Dynamics of magnitudes of integral spatial depolarization (NQRS) and repolarization (NT) vectors in cosmonauts after flight.

Here and in Figures 2 and 3: solid line refers to preflight data, dash line to preflight period and line with circles to postflight data

Postflight studies [7, 8] revealed changes in some biochemical parameters: increased excretion of 17-HCS [hydroxycorticosteroids] in urine with concurrent increase in free 17-HCS in the first crew, as well as decline of potassium content of the body and of some enzymes in blood. These changes, which were an indirect indication of possible development of stress and metabolic changes in the myocardium, could be instrumental in impairing the repolarization process. However, the changes we observed on the EKG do not enable us to relate them specifically to changes in levels of some electrolytes or other in the body.

The magnitude of the vector of ventricular myocardial depolarization did not usually undergo appreciable changes after the flight and only in the CDR-1 did it usually exceed the maximum preflight value of this parameter from the day of landing up to the 33d day (see Figure 1). The absence of marked changes in integral QRS vector (at any rate, absence of decline thereof) indicates that there were apparently no appreciable disturbances of the depolarization process under the influence of flight conditions. This is, perhaps, related to the fact that some physical exercise was performed regularly during the flight. Moreover, the increase in cardiac output demonstrated during the flight (by the rheographic method), appearance of signs of volumetric load on the heart and increase in its absorptive function (according to phase analysis data) are apparently related to displacement of fluid in a cranial direction and decreased load on muscles, leading to diminished activity of "peripheral muscular hearts" [9], and they can be interpreted as adaptive reactions instrumental in maintaining the conditioned state of the myocardium.

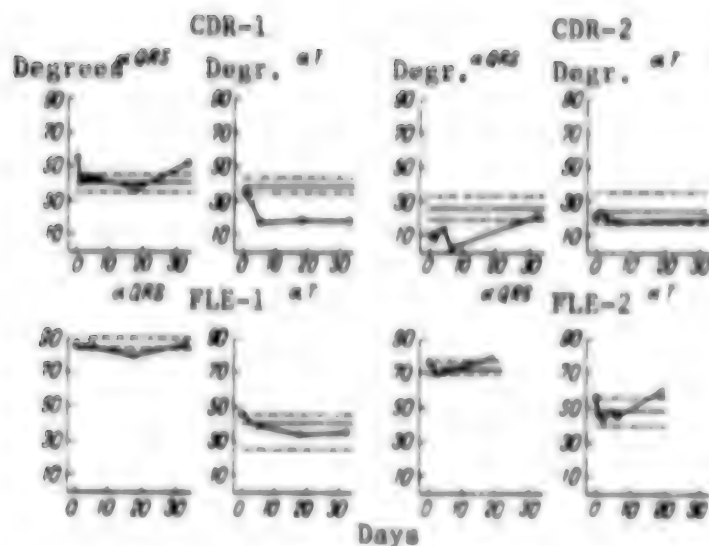


Figure 2.
Dynamics of magnitude of angles α_{QRS} and α_T determining the direction of projections of corresponding integral vectors in the frontal plane

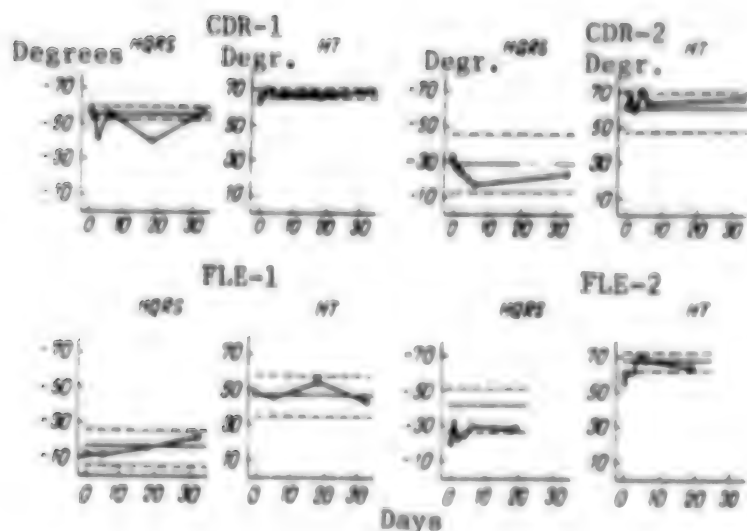


Figure 3.
Dynamics of magnitude of angles H_{QRS} and H_T determining the direction of projections of corresponding integral vectors in the horizontal plane.

Negative values of H_{QRS} show that the vector is directed behind the frontal plane

An appreciable change in position of projection of $\bar{H}_{QRS}$ on the frontal plane was noted only in the CDR-2 in the form of a 15-24° decrease in α_{QRS} , as compared to preflight data (Figure 2). The decline of this parameter persisted for 1 month.

Angle H_{QRS} was negative before and after the flight in all of the cosmonauts and, as a rule, it diminished in the postflight period (in 3 of the cosmonauts; in the CDR-1 it diminished only on the 2d and 18th days) (Figure 3).

The position of the projection of vector T in the frontal plane changed appreciably only in CDR-1, with an overt tendency toward decrease in α_T by the 5th day, with persistence of low value through the 33d day (see Figure 2). As a rule, angle H_T corresponded to preflight values, and it diminished only in FLE-2 for the first 2 postflight days (see Figure 3).

Thus, the most appreciable change was the marked decline in magnitude of the integral vector of repolarization on the day all of the cosmonauts landed, and it did not return to its proper value for 1 month of the postflight period in 3 of them, as well as a tendency toward shifting forward of the integral vector of QRS in 3 cosmonauts in the postflight period. According to the submitted results of our study, the changes in vector MI are primary, and perhaps they are related to the vegetative unbalance that developed in flight and vegetative myocardial changes that first affect the more labile repolarization process. At the same time, regular exercise, increase in volumetric heart load and diminished activity of "peripheral muscular hearts" are probably factors which prevent development of appreciable changes in the process of myocardial repolarization. On the whole, our studies revealed that the changes in bioelectrical activity during the flights were not clinically meaningful, did not affect hemodynamics or health status of the crews.

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UDC: 629.78:612.395:[613.2:547.96

CONFORMITY WITH HUMAN REQUIREMENTS OF PROTEIN CONTAINED IN THE RATIONS FOR CREWS OF THE SALYUT-6 ORBITAL STATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981 pp 26-29

[Article by V. P. Bychkov, A. K. Sivuk and I. I. Borodulina, submitted 14 Apr 80]

[English abstract from source] Nitrogen metabolism in 16 test subjects and 8 cosmonauts kept on a diet containing dehydrated products and foodstuffs preserved by other methods (15% and 85%, respectively) was studied. The health state and excretion of end-products of nitrogen metabolism in those people gave evidence that the dietary protein met well bodily requirements under normal conditions, in simulated flight, and in real flight aboard Salyut-6.

[Text] One of the main prerequisites for preserving health and maintaining a high degree of efficiency is an adequate supply of the main plastic component of food, first-class protein, for man during space flights. To meet this condition, one must have a clearcut idea both about the biological value of proteins contained in foods included in the onboard rations and human protein requirements in the presence of space flight factors [1-11].

Our objective here was to assess the adequacy to human requirements of the proteins supplied in the diet for crews of Salyut-6, which consist of a combination of dehydrated foods (15%) and products preserved by other methods (85%).

Methods

Data were obtained from 3 series of tests conducted on 16 male volunteers and 8 cosmonauts.

The daily diet consisted of the following (mean amounts given): 138.0 g protein, 99.0 g fats, 360.0 g carbohydrates (1:0.7:2.6), 61.3 g moisture, 22.2 g ash; mean caloric value constituted 3000 kcal (12,550 kJ).

In the first series, we determined the adequacy of the protein component of the diet to human requirements under ordinary living conditions. We tested 10 people who performed their routine work throughout the period of the study (60 days). In the second series, we assessed the adequacy of the protein component to human requirements when subjects were kept in a pressure chamber in a ground-based

research complex. Six men participated in this test; they had undergone a physical and were deemed to be in good health. Their stay in the chamber varied, ranging from 18 to 120 days. During this study, the carbon dioxide content in the pressure chamber was altered (12th-34th and 55th-90th days). The concentration of carbon dioxide in the atmosphere was increased (to 1.5-2.5%) by changing the number of people in the chamber from 3 to 4 (simulation of "visiting expedition"). Physical exercises constituting energy expenditure of 400-450 kcal/day were scheduled to prevent the hypodynamic syndrome.

In the third series, we assessed the adequacy of the protein in the diet to human requirements in the course of actual space flights, for which purpose we examined crews of the first two main expeditions and two "visiting expeditions" (Soyuz-30 and Soyuz-31) to the Salyut-6 orbital station. They were examined in the preflight and postflight periods.

In order to assess protein metabolism, we assayed the following end products of nitrogen metabolism in 24-h urine: total nitrogen, urea, ammonia, aminonitrogen, uric acid, creatine and creatinine. We also examined nitrogen balance.

Results and Discussion

The results of the first series of tests revealed that 60-day intake of the on-board diet under laboratory conditions did not affect the levels of excretion of end products of nitrogen metabolism in urine. Excretion of total nitrogen in urine ranged from 15.0 ± 0.28 g/day to 16.5 ± 0.65 g/day. Urea excretion did not exceed the physiological range and constituted a mean of 29.3 ± 1.30 g/day ($85.6 \pm 1.67\%$ of total urine nitrogen). Ammonia excretion ranged from 1.02 ± 0.06 to 1.22 ± 0.02 g/day ($5.5-5.8\%$ of total nitrogen) and aminonitrogen from 0.29 ± 0.02 to 0.44 ± 0.02 g/day ($2.5 \pm 0.06\%$ of total nitrogen). There was a positive nitrogen balance (mean of $+2.13 \pm 0.355$ g/day) throughout the period of the study. Individual fluctuations of this parameter ranged from $+0.87$ to $+4.69$ g/day).

Thus, these data indicate that the tested diet maintained a normal level of nitrogen metabolism in 10 subjects who stayed on this diet for 60 days under laboratory conditions, and that the protein content met body requirements.

The results of the second series of studies revealed that a normal level of excretion of total nitrogen and its components persisted for most of the time spent in the pressure chamber, regardless of duration of the subjects' stay in this chamber. The observed individual fluctuations of tested parameters were in the following ranges: 12.4-19.4 g/day total nitrogen, 25.0-35.0 g/day urea, 0.61-1.68 g/day ammonia, 0.73-1.39 g/day uric acid, 0.64-2.16 g/day creatinine. Nitrogen balance remained positive, fluctuating from $+2.13$ to $+6.54$ g/day. Exposure to high carbon dioxide content in the atmosphere of the chamber did not affect nitrogen metabolism, whereas at the times of "changing crews" there was some increase in excretion in urine of total nitrogen, urea and ammonia, with decline of positive nitrogen balance. The demonstrated changes were probably attributable to the nervous-emotional stress that the subjects developed at these times.

In view of the fact that the fluctuations of the tested parameters of nitrogen metabolism did not exceed the range of the conventional physiological norm, it can be concluded that the protein content in the diet used met human requirements when simulating space flight factors in the pressure chamber.

The results obtained from studies of parameters of nitrogen metabolism in crews of Soyuz-30 and Soyuz-31 were characterized by the patterns inherent in short-term space flights. The degree of change was more related to the individual distinctions of each cosmonaut. However, more marked changes in the same direction were demonstrated in the crew of Soyuz-30, as manifested by a 30% decline in excretion of total nitrogen, as compared to the base level, 33% decline in excretion of urea and 18% decline for ammonia. There was only negligible decrease in excretion of aminonitrogen, ammonia and uric acid in the crew of Soyuz-31. These changes could be related to general fluid retention and consequent decrease in 24-h diuresis in the postflight period. It should be noted that 24-h diuresis constituted a mean of only 60% of the preflight level in the crew of Soyuz-30.

Examination of nitrogen metabolism in the crew of the first main expedition aboard Salyut-6 (96-day mission) revealed that, in spite of individual fluctuations in excretion of end products of nitrogen metabolism in the postflight period, their range was within preflight levels. Excretion in urine of total nitrogen in the crew of the first main expedition, which constituted 11.1 g/day on the 1st postflight day, was close to preflight levels (11.6 g/day); on the 3d-4th postflight day it dropped to 9.0 g/day, then reverted to the base level (5th-7th day).

The results of examining nitrogen metabolism in the crew of the second expedition aboard Salyut-6 orbital station (140-day mission) revealed that excretion of the end products of nitrogen metabolism was close to preflight levels (5th-3d day before lift-off) in the postflight period (1st-2d day after landing). On the 3d postflight day, there was a 40% decrease in excretion of total nitrogen, 21% decrease for urea and 44% decrease for ammonia, with retention of normal proportion. There was a tendency toward normalization of these changes on subsequent postflight days.

Analysis of the results of studies of nitrogen metabolism in the crews of Soyuz-30, Soyuz-31 and of the two main expeditions aboard Salyut-6 as a whole leads us to conclude that the changes in parameters of nitrogen metabolism in the preflight period occurred under the influence of nervous and emotional stress, whereas in the postflight period they were apparently related to compensatory nitrogen retention following some loss thereof during the flights. The range and direction of the changes were related to individual distinctions of the cosmonauts and degree to which they followed the planned set of preventive measures. The physical status of the cosmonauts [12] and parameters of nitrogen metabolism after the missions were indicative of adequate intake of first-class protein as part of the onboard rations developed for crews of the Salyut-6 orbital station, consisting of foods that were dehydrated and preserved by other methods.

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STATE OF COSMONAUTS' ADRENHYPOPHYSEAL SYSTEM FOLLOWING ORBITAL FLIGHTS OF
DIFFERENT DURATION

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
pp 29-32

[Article by V. B. Noskov, I. S. Balakhovskiy, A. I. Grigor'yev, I. G. Dlusakaya and
R. K. Kiselev, submitted 11 Nov 79]

[English abstract from source] In order to assess the hypophyseal-adrenal system and glucocorticoid activity, excretion of total 17-hydroxycorticosteroids (17-HOCS) was measured before and at R+1 day after a standard water load (20 ml/kg). Twenty-six cosmonauts were examined after flights of 2-140 days. Although the cosmonauts spent different time in weightlessness, the content and rate of glucocorticoid excretion in the urine during postflight water loads was 1.5-2 times higher than during preflight loads. This increased excretion of 17-HOCS was associated with their decreased reabsorption and/or increased glomerular secretion. The latter may be a manifestation of extrarenal action of ACTH due to its hyperproduction immediately postflight.

[Text] Increasing attention is being given by specialists to man's hormonal status in weightlessness and in the period of readaptation following space flights in view of the increased duration of space expeditions. Under these conditions, some authors observed increased excretion of 17-hydroxycorticosteroids (HCS) in urine [1, 2], while others observed a marked decrease in excretion of these hormones both during [3, 4] and on the 1st day after [5] space flights. Thus, studies of levels of hormones and their metabolites in urine without functional loads did not always yield unequivocal results. We tried to assess the state of the adrenohypophyseal system by means of the water load test, which is one of the clinical methods of examining fluid-electrolyte homeostasis, renal function and adrenal activity. This test was first used in a postflight examination of the crew of the Voskhod spacecraft [6], and was subsequently performed after virtually every orbital flight.

The results of assaying the concentration of glucocorticoid hormones in blood depend largely on the time of taking a blood sample for the test, since secretion thereof is irregular and episodic [7-9]. For this reason, to assess activity of the adrenal cortex it is much more reliable to examine corticoid excretion in urine. However, in this case, one must take into consideration that not only active hormones, but metabolites thereof are excreted in urine, and the amount and composition of the latter depend both on secretory activity of the gland and

metabolic processes, as well as renal capacity to excrete these substances. The water test creates optimum and standardized conditions for renal function. Moreover, a rather high diuresis lowers methodological errors due to the presence of so-called dead space in the urinary tract and residual urine in the bladder.

There has been repeated publication of the results of testing renal function in cosmonauts with the use of this test [5, 10, 11]. Our objective here was to examine excretion of adrenocortical glucocorticoid hormones with the water test, which was performed after completion of space flights lasting 2 to 140 days.

Methods

The standard method [12] was used to conduct the water test on a fasting stomach, in the morning, on the 2d postflight day.* After drinking water in an amount corresponding to 2% of body weight (20 ml/kg) all at once, urine was collected in separate batches for 4 h, and assay was made of levels of total (free and glucuronide) HCS after enzymatic hydrolysis using a modification of the Silber-Porter method [13]. The water test was similarly conducted on all cosmonauts, as well as their back-ups during preparations for the flights. The data were submitted to statistical processing, and they served as a control to evaluate postflight findings.

Results and Discussion

In spite of the fact that the duration of the space flights varied, all of the cosmonauts examined presented consistent changes in excretion of HCS during the water test (Table 1). After termination of both 2-5-day orbital flights and 6 months in weightlessness, there was the same, approximately 1.5-2-fold increase in excretion of total HCS during the water test, as compared to the preflight level. This enabled us to group all of the obtained data and submit them to statistical processing to assess the general physiological patterns of this reaction. On the average, the concentration of total HCS in urine almost doubled (Table 2) during the postflight water tests, as compared to the control level, while the amount of corticoids excreted during the test and rate of excretion increased by 71 and 79%, respectively. There was also an increase in postflight concentration of hormones and excretion thereof at peak diuresis during the water test, although maximum diuresis changed insignificantly, or even diminished. The independence of this reaction from duration of exposure to weightlessness was confirmed when we compared the levels of HCS excretion in cosmonauts who participated in repeated orbital flights differing in duration. Table 1 shows that the water load increased excretion of total HCS, regardless of duration of space flights. There was typical individualization of HCS concentration in urine during the water test. For example, the differences in rate of excretion of glucocorticoids after different flights in cosmonaut No 19 were not attributable to a change in hormone concentration, but in diuresis levels.

Glomerular filtration and reabsorption-secretory activity of renal tubules are also actively involved in excretion of corticosteroids in urine. Most of the conjugate HCS, passing through the glomerular filter, are excreted in urine [14-16] and, conversely, 80-96% of the free glucocorticoids that have passed into the ultrafiltrate are reabsorbed in the renal tubules [16-18]. There are also data

*B. R. Dorokhova and B. V. Morukov also participated in conducting several of the water tests.

indicating that the glucuronides of corticosteroids can be actively secreted in the proximal tubules of the nephron [19, 20].

Table 1. Concentration and excretion of total 17-HCS and fluid during water tests performed on cosmonauts following orbital flights of different duration

Cosmo- naut No	Flight time, days	HCS excre- tion, mg/h	HCS concentra- tion μg/ml	Maximum diuresis ml/min
1	2	0.53	2.80	10.5
2	2	0.57	2.80	15.2
3	2	1.23	2.0	12.8
4	2	0.87	1.80	12.3
5	5	0.58	2.30	16.7
6	5	0.46	1.90	8.3
7	5	0.66	2.50	9.5
8	5	0.78	4.70	6.2
9	5	0.89	3.0	9.5
10	5	0.53	1.80	16.0
11	5	0.32	1.70	14.2
12	8	0.73	2.60	5.8
13	8	0.65	2.20	17.0
14	15	0.63	2.40	11.5
15	15	0.75	6.05	10.7
16	18	1.10	2.20	10.2
17	18	0.35	5.80	—
9	18	0.65	3.80	—
18	30	0.92	2.70	7.7
19	30	0.37	1.40	6.5
12	62	0.79	2.50	6.2
16	62	0.64	2.40	7.0
20	96	0.65	2.05	15.2
19	96	0.89	1.80	22.3
21*	140	0.59	2.30	—
22*	140	0.77	2.20	—

Note: The values for excretion and concentration of 17-HCS are the means per test. Asterisks refer to the water-calcium test.

After termination of the space flight, no appreciable change was usually noted in rate of glomerular filtration [21, 22]; consequently, the increased rate of excretion of total HCS in urine after the water test, conducted in the postflight period, could be attributed to diminished reabsorption thereof and/or increased secretion in the renal tubules.

In previous studies [23, 24], we demonstrated that the magnitude of HCS excretion in urine against the background of water diuresis depends on the level of secretion of adrenocorticotrophic hormone (ACTH) and glucocorticoid activity of the adrenals. In this connection, the increase we demonstrated in excretion of glucocorticoids during the postflight water test could have been caused by rather severe nervous and emotional stress. In this study, the water tests were performed 40-45 h after the crews landed, after the period of severe emotional and physical stress related to termination of the mission. At this time, the cosmonauts were in a comfortable hospital, they had had 8-9 h of calm sleep, and the water test did not elicit any negative attitude or any emotional experiences on their part.

Table 2. Excretion of fluid and total HCS during water tests conducted on cosmonauts before and after flights of different duration, M±m

Parameter	Preflight (n = 35)	Postflight (n = 26)
17-HCS		
Concentration, µg/ml	1.36±0.07	2.74±0.24
Excretion in 4 h after test, mg	1.44±0.07	2.39±0.14
Excretion rate, mg/h	0.39±0.01	0.70±0.04
Fluid		
Maximum diuresis, ml/min	12.2±0.4	11.5±1.0
Water load excretion, %: in 2 h	65±3	51±4
in 4 h	87±3	65±5

The results of postflight water tests may also be indicative of inadequate intensification of ACTH secretion during this period and of its extraadrenal action, i.e., direct influence of the tropic hormone on the kidney, intensifying HCS excretion in urine. In our opinion, this could occur by means of intensification of corticosteroid glucuronides in the proximal tubule of the nephron. Both a decrease and increase in blood ACTH were noted in American astronauts after their return to earth [25, 26], and the increase was not always associated with adequate increase in concentration of hydrocortisone [27]. These data are consistent with our hypothesis. Along with the nervous and emotional factors, the cause of increased ACTH production could be, in particular, an increase in secretion of antidiuretic hormone (ADH) which, according to some authors [28-30] is a physiological regulator of ACTH secretion. An increase in ADH content of urine and blood of cosmonauts in the postflight period has been reported repeatedly [10, 31, 32]. Moreover, there are data indicative of diminished functional activity of the adrenals in weightlessness [5, 33], whereas with hypofunction of the adrenal cortex there is, as we know, an increase in ACTH production [34, 35]. Impaired metabolism of glucocorticoids in weightlessness and unbalance in the so-called feedback system, which regulates secretion of this tropic hormone, may also be the possible causes of ACTH hyperproduction.

The above is only one of the hypotheses that summarize and combine the accumulated data. Further special studies are required, in particular, with the use of hormone load tests, in order to substantiate this hypothesis completely and to demonstrate the true mechanisms of hormonal changes in weightlessness and during the period of readaptation to earth.

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EFFECTS OF SPACE FLIGHTS ON LYMPHOCYTE BLAST TRANSFORMATION IN COSMONAUTS'
PERIPHERAL BLOOD

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pp 32-34

[Article by A. T. Lesnyak and R. Yu. Tashpulatov, submitted 5 May 80]

[English abstract from source] The postflight investigation of cell mediated immunity of seven cosmonauts showed significant increase in spontaneous activity of lymphocytes of peripheral blood and decrease in stimulation of lymphocytes cultured with PHA at R+0. Variations in these parameters were transient, remaining within physiological limits. Two cosmonauts displayed a stable increase in lymphocyte activity during blast transformation test with *Staphylococcus aureus* culture filtrate.

[Text] The period of cosmonaut readaptation to earth after a space flight is characterized by a change in some parameters of humoral immunity. The previously published data are indicative of an increase in serum complement C_{3c} and C₄ factors, change in levels of some serum proteins (haptoglobin, G_c globulin, ceruloplasmin), increase in serum immunoglobulins IgA, IgG and IgM [1] and appearance, in a number of cases, of antibodies against the human myocardium [2].

Our objective here was to examine the nature and degree of functional impairment of cellular immunity in cosmonauts during the readaptation period (1 month) using the blast transformation reaction of peripheral blood lymphocytes.

We submit here the results of examining 27 individuals from a detachment of cosmonauts and 7 cosmonauts who had participated in space flights aboard Salyut-24--Salyut-5, Soyuz-26, Soyuz-27 and Soyuz-28--Salyut-6.

Methods

For the blast transformation reaction, we used a method that was described previously [3]. We selected PHA-M [phytohemagglutinin] (Difco Co., United States) and filtrate of a *Staphylococcus aureus* culture (SF) as mitogens. The results of the reactions were evaluated according to level of incorporation of ³H-thymidine in lymphocyte DNA, and they were expressed as the index of stimulation (IS), which was the ratio between number of impulses/min in cultures with and without mitogen, and which yields similar results when using different methods to evaluate the reactions [4].

Results and Discussion

The mean parameters of the blast transformation reaction in 27 men who were undergoing professional training in the cosmonaut detachment constituted 163 ± 13 pulses/min without mitogen, 113 ± 10 with PHA (IS) and 7.4 ± 1.3 with SF (IS). The results of these studies were used to evaluate fluctuations of parameters of blast transformation reactions in cosmonauts who had completed space flights.

The cosmonauts were examined before the flights and during the period of readaptation to earth. On the 1st postflight day we observed an increase in uptake of H-thymidine in lymphocyte cultures without mitogen from 119 ± 13 to 197 ± 29 pulses/min ($P < 0.05$) and in cultures with PHA from $20,180 \pm 410$ to $26,210 \pm 7290$ ($P > 0.05$). Against this background, there was some decrease of IS in the lymphocyte cultures with PHA, as compared to the preflight level (164 ± 26 before and 119 ± 24 after the flight; $P > 0.05$); however, it remained in the normal range. Although the mean value of IS was unreliably lower in lymphocyte cultures with PHA, the decline on the 1st postflight day was noted in all 7 cosmonauts, and apparently it was related to increased spontaneous lymphocyte activity.

At the subsequent stages of the readaptation period all of the examined cosmonauts presented restoration of IS to either the base level, or somewhat higher values in cultures of lymphocytes with PHA.

In individuals who had a normal preflight IS level, the lymphocyte blast transformation reaction in cultures with SF failed to demonstrate significant fluctuations after the flight.

In two cosmonauts, who had a high IS before the flight, the dynamics of changes in this parameter in the readaptation period varied. In one of them, IS, which constituted 20.0 before the flight did not exceed 6.2 after it. It is only when this cosmonaut was examined 6 months later that we observed elevation of IS to 22.7. In the other cosmonaut, IS constituted 74.4 on the 1st postflight day, versus 63.4 as the preflight value. In this case, IS was above normal levels in cultures of lymphocytes with PHA, both before and after the flight.

These results indicate that there was some drop of IS in lymphocyte cultures with PHA on the 1st postflight day, which is consistent with the findings of other authors [5, 6]. The deviation of IS did not exceed the normal range, and it soon reverted to preflight values, i.e., it was reversible and functional in nature. We demonstrated that the diminished capacity of peripheral blood lymphocytes for PHA stimulation on the first postflight day was related to high spontaneous activity of lymphocytes. This is in contradiction with data in [6], which indicate a decreased incorporation of radioactive tracer in cultures of peripheral blood lymphocytes of astronauts who participated in the flight aboard Skylab-3. On the other hand, an increase in spontaneous activity of rat lymphocytes in in vitro cultures was reported in the experiment aboard Cosmos-782 biosatellite [7].

We were unable to relate the difference in peripheral blood lymphocyte reactions in cultures with SF to any factors. Moreover, the question of nature of stimulation of lymphocytes by SF has not yet obtained a complete answer. It should be noted that the high IS in lymphocyte cultures with SF was stable.

Thus, during the period of readaptation to earth after space missions, cosmonauts presented brief change in peripheral blood lymphocyte functions, manifested by an increase in spontaneous activity and some decrease in capacity for blastogenesis under the influence of PHA. In two cases, there was a persistent increase in lymphocyte activity in cultures with SF before and after the space flight. Further studies must be pursued to determine the causes of fluctuations of parameters of cellular immunity.

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CHANGES IN BODY MASS OF COSMONAUTS IN THE COURSE OF A 140-DAY SPACE FLIGHT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
pp 34-36

[Article by A. D. Yegorov, I. I. Kas'yan, A. A. Zlatorunskiy, S. F. Khlopina, V. A. Talavrinov, I. A. Yevdokimova, Ye. M. Romanov and V. I. Somov, submitted 23 Feb 80]

[English abstract from source] During 140-day space flight body mass changes of the Commander and Flight-Engineer were measured. No correlation between body mass losses and flight duration was found. Greatest body mass losses occurred on MD 44-59 in Commander (2.3-2.4 kg) and on MD 86 in Flight-Engineer (5.4 kg). Later the losses decreased. The results suggest that body mass changes varied on an individual basis and depended on many spaceflight factors.

[Text] Body mass studies were made after all space missions. It was demonstrated that a decrease therein was unrelated to duration of the flights, and that it could reach 6 kg. In view of the possible link between reduction in body mass in flight and fluid loss, it was deemed purposeful to investigate the dynamics of this parameter in crew members during space missions. Such studies were first conducted aboard the orbital stations, Skylab [1] and Salyut-5 [2], and they were continued on Salyut-6 (second expedition).

Methods

The inertial properties of the body were used to measure the body mass of any object in weightlessness [3]. Technical execution of the necessary instrument was based on a linear, one-dimensional harmonic oscillator.

In view of the fact that the human body is a mechanical system consisting of solid structures and semiliquid mass, it can be approximated at low frequencies and low levels of vibration by a linear system with a finite number of degrees of freedom (3). The presence of resonance frequencies in the "chest--abdominal cavity" region (from 3 to 6 Hz) determined our choice of the range of 0.3 to 0.5 Hz for measurement of frequencies.

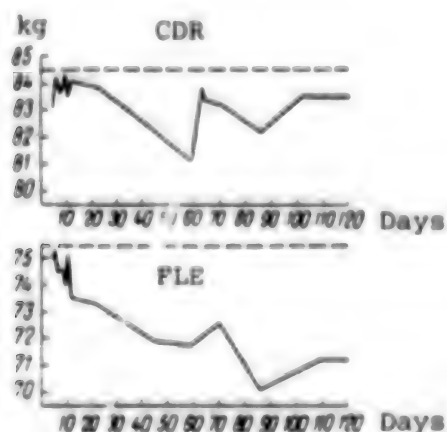
To improve the accuracy of measurements, the cosmonaut assumed a position that enabled him to regulate the closeness of contact with the mass meter platform. The cosmonaut was positioned in prone position on the platform, with the chin propped on a movable rest (to immobilize the head), the hands on levers and

the feet on footrests. The movable part of the instrument was pulled to the bottom fixed position with a knob on the base of the instrument. Upon depressing with the fingers the release hooks, the movable part began to oscillate, and body mass was determined from the period of oscillations. Before measuring mass, the instrument was calibrated and its technical condition checked by measuring the period of oscillation of a standard [reference] mass (the movable part of the instrument). Body mass was measured while the subject held his breath and tensed his muscles.

Results and Discussion

Body mass was measured daily from the 4th through the 11th days of the mission. Thereafter, it was measured about once every 2 weeks.

On the 4th day of the flight, body mass was diminished, as compared to preflight levels: by 1.4 kg in the crew commander (CDR) and by 0.55 kg in the flight engineer (FLE) (see Figure). Thereafter, not only did the body mass loss fail to increase in the CDR (up to the 22d flight day), it even decreased and constituted 0.31-1.03 kg. From the 44th through the 59th day of flight, the CDR presented an increase in mass loss to 2.3-3.4 kg, whereas on the 63d-122d day it constituted only 0.7-1.6 kg. The dynamics of body mass for the FLE during the mission differed and were characterized by progressive increase of loss to the 86th flight day. At this time, the body mass of the FLE was 5.4 kg lower. Thereafter, the loss of body mass gradually decreased and constituted 3.8 kg by the 122d flight day. There was postflight restoration of body mass within 3 days for the CDR and 2 weeks for the FLE.



Dynamics of body mass in the second main crew during the mission. Solid line--parameter in flight; dash line--mean value before flight

When analyzing the dynamics of body mass during flights, one must take into consideration a number of factors which, as will be seen from the data submitted below, had some influence on changes therein. The EVA [extravehicular activity] operation, which involved working in space suits outside the spacecraft, was associated with 0.7 kg loss of body mass by the CDR and 0.85 kg loss by the FLE. Performance of exercises in onboard gear also caused some decline of this parameter, as indicated by control measurements taken by the CDR before and after exercises on the 63d and 64th days of the mission, which revealed that there was approximately an 0.6 kg weight loss under the influence of exercise. Finally,

one should also take into consideration the role of the metabolic factor, which is related to food intake. This was indicated most graphically by data on the dynamics of body mass of the FLE during the period from the 86th through 122d days of the mission. Analysis of the situation on the 86th day of the mission, when loss of body mass constituted 5.4 kg in the FLE, revealed that he did not consume all of the daily rations, the caloric value of which was about 3100 kcal/day due

to selective decrease in appetite for some foods. For this reason, it was recommended that three rations be used by the crew daily, so that the assortment of foods could be more varied. This measure, as well as delivery of foodstuffs by the freight craft, Progress-4 (with due consideration of the wishes of the crew), resulted in reducing the weight loss of the FLE from 5.4 kg on the 86th day to 3.8 kg on the 122d.

Finally, it must be borne in mind that the intensity and duration of exercises performed by the FLE were smaller, though rather large, than those performed by the CDR. This circumstance could have resulted in greater loss of muscle mass, which was confirmed, in particular, by the slower recovery of body mass in the FLE after the mission.

To sum up the foregoing, it can be concluded that there was no clearcut correlation between body mass loss and flight duration during the mission in the CDR. The most marked decline of this parameter was observed on the 44th-59th days and constituted 2.3-2.4 kg, not exceeding 1.7 kg at other stages of the mission (86th day). The body mass of the FLE diminished progressively up to the 86th day of the mission (by a maximum of 5.4 kg); the mass loss diminished thereafter, after replacement of some foods for which there was selectively less appetite. The study of body mass during the 140-day mission leads us to assume that the following are the principal factors that could cause loss of body mass: redistribution of body fluids which, according to current conceptions, leads to loss of some part of the fluid; high degree of physical activity; inadequate compensation of metabolic losses by the food rations, which could occur for different reasons; diversity of stress factors, in particular the emotional stress during important operations (such as EVA or descent of spacecraft); loss of muscle mass as a result of inadequate overall exercise of the muscular system or different muscle groups.

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STUDY OF MASS-INERTIA CHARACTERISTICS OF HUMAN BODY SEGMENTS DURING 6-MONTH HYPOKINESIS BY THE GAMMA SCANNING METHOD

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981 pp 36-42

[Article by V. A. Tishler, V. M. Zatsiorskiy and V. N. Seluyanov, submitted 6 Sep 79]

[English abstract from source] It was found that there is a distinct redistribution of body masses in 18 test subjects exposed to 6-month hypokinesia. Six of them (who did not exercise) showed losses of muscle mass (primarily antigravity muscles) and gain of adipose mass, and 12 test subjects (who exercised as a counter-measure against hypokinetic effects) displayed insignificant losses of muscle mass and significant gain of adipose mass.

[Text] Several methods have been developed to date that permit indirect determination of the mass of segments of the human body: immersion in water, stereophotogrammetric, mathematical and physical modeling [1, 2]. However, these methods have substantial flaws. Indirect determination of mass from volume requires knowledge of density of segment tissues, and such data can be obtained only on cadavers.

The work pursued in the problem laboratory of the State Central "Order of Lenin" Institute of Physical Culture (GTSOLIFK) made it possible to develop a radioisotope method of determining mass-inertia characteristics of human body segments. In developing this method, it was necessary to achieve accuracy of over 3-4% in determination of mass-inertia characteristics for a large number of body segments with minimal exposure of the subject to radiation (less than 0.01 rad).

The studies were conducted on a special device consisting of an electromechanical and electron part (see Figure). The electromechanical part consists of table 14, carriage 10 and control console 7. The object to be measured 15 is placed on the table. When the motors on legs 13 are turned on, the table starts to move over track 12. The carriage also has four motors 22 and it can move on track 11, which is perpendicular to track 12, over which the table moves. A light-weight rod 18 is attached to the carriage, and the source of radioactivity 17 is placed in a capsule at the end of this rod. As a result of the simultaneous advancing movement of the table and back-and-forth movement of the carriage, the isotope moves over the subject's body in a zigzag trajectory.

The electronic part of the equipment consists of a scintillation detecting unit 19 (with NaI crystal), 150 mm in diameter and 100 mm in thickness, of integral construction, analyzer 1 and 2 (Va-V-100), converter [scaling, converting instrument] 3 (VA-I-120) and punch 4.

There is a lead shield 20 (11 cm thick) over the detector with a rectangular collimating opening (3x18 mm).

During the scan, the intensity of the penetrating beam of γ -radiation is recorded on papertape [punched tape] at a frequency of 1.2 s. In the course of the scan, the coordinates of different body segments are fixed by means of a light switch from a system of mirrors that are attached to the end of the rod under the isotope.

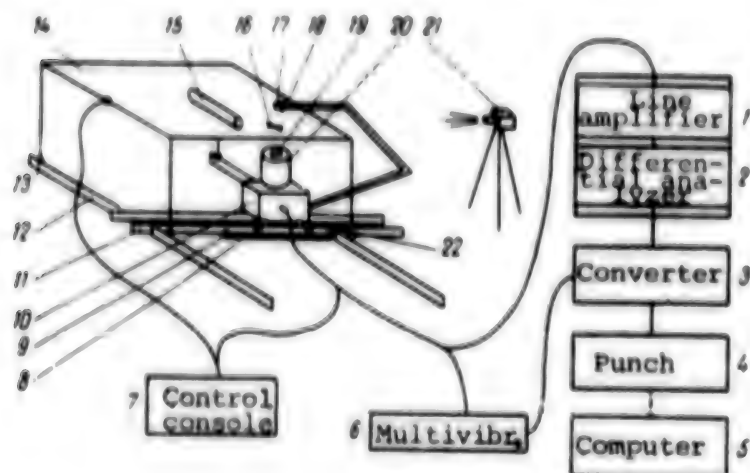


Diagram of unit for γ -scanning. Key is explained in the text.

For our study we selected the following parameters for the device: 2.2 cm/min movement of table, 70-cm scan by carriage with 2 cm/s rate of carriage movement, 1.3×2.4 cm² size of single stage and, in the case of a scanning area of 40 cm, 0.73×2.4 cm². If one were to scan first all parts of the body (from head to feet, scanning area of 70 cm), then the hands and feet, 40-cm scan), the time required to examine an individual 170 tall would be 2.5 h. On the basis of the above conditions and maximum dosage of 0.001 for exposure of the subjects, we calculated the activity of ^{137}Ce isotope. It did not exceed 250 μCi . In this case, the radiation dose to the subject is 500 times less than the permissible maximum, while an operator would be exposed to 0.01 rad over a year of work (8-h work day) at a distance of 2 m from the source of γ -radiation.

The method used to determine the geometry of human body mass on this apparatus consisted of the following elements: 1) weighing and determining the general center of gravity (GCCG); 2) anthropometric measurements; 3) calibration of equipment; 4) adjustment of electromechanical part; 5) positioning subject on the table in the appropriate position; 6) giving instructions to the subject; 7) turning the device on (and obtaining coordinates of the main anatomical points). Since the subject is scanned in parts (body without hands and feet, then the hands and feet separately), items 3-7 were repeated each time the position was changed. The information punched on the papertape about intensity of γ -radiation was processed on a computer [5].

On the whole, the method used for anthropometric measures corresponded to the second system of V. V. Bunak (with some additions) and consisted of measuring body mass, body length in supine position, GCG (in two positions), foot size (4 measurements), height of points from the floor (12 measurements), girths (12 measurements) and cutaneous fat folds (12 measurements).

Determination was made of the coordinates of 10 segment* when scanning each subject: head, top part of the trunk, middle of the trunk, lower trunk, thigh, leg, foot, arm, forearm and hand. The choice of reference points for the boundaries of the segments was determined by biomechanical requirements: the beginning and end of a segment had to coincide with the axis of rotation in the joint, while the mass of the segment had to remain constant during the examination. One can check whether optimum segmentation has been made after including mass geometry data in mathematical models. The results of estimates made on these models can be compared to analogous data obtained after dividing the body into segments. It should also be noted that the method we used to separate into segments takes into consideration the historically developed method of separating cadavers into parts, and this makes it possible to compare the results with the data of other authors.

This study was conducted on 18 essentially healthy male volunteers ranging in age from 36 to 40 years, who spent 182 days under antiorthostatic [head tilted down] hypokinetic (AOH) conditions with the head tilted down at an angle of -4.5° . The subjects were divided into three groups: the first (control) consisted of six men who were submitted to AOH without the use of preventive measures; the second group ("regular" [?]) consisted of six men on whom a set of preventive measures was used: specially organized, regular exercise, myoelectrostimulation (30-day courses every other day with 15-day intervals between courses) and, at the final stage, LBNP [lower body negative pressure] conditioning and salt supplement. They exercised in horizontal position twice a day, for 1 h each time, on a special exerciser that enabled them to pedal and row [with oars] (with automatic, programmed control of exercise load), as well as running and walking in one place. The calories expended on exercise ranged from 300 to 400 kcal/h in different subjects. The nature and method of this set of measures corresponded to the one that is used on the Salyut stations; the third group of subjects (6 men) performed the same exercises without myoelectrostimulation; however, the periods with less exercise (3 times a week) but with greater intensity of exercise alternated with periods of the same volume and greater intensity of exercise. The period with the greater load also coincided with the last 3 weeks of AOH.

Results and Discussion

The data obtained in the course of the anthropometric examination and scanning were processed on a computer. We calculated the mass-inertia characteristics of 10 segments of the body, determined their statistical ratings, as well as statistical ratings of anthropometric signs. In all, we processed 222 signs, including the length of different parts of the body, girth, diameters, fatty folds in the skin, data on composition of body, absolute and relative mass-inertia characteristics of body segments.

Since the examinations were performed twice (before and after 182-day AOH), we analyzed the differences between the recorded signs. In this case, the *t* criterion of Student is considered to be the most adequate and statistical, and it is

*While scanning, determination was made of coordinates of anthropometric points defining segment boundaries by means of light crossing 16. The latter was formed by projection of light beam 21 on the mirror system at the end of the rod 18.

calculated with consideration of the assumption that the mean values, between which differences were found, were calculated from interdependent samples.

Calculation of the *t* criterion for all 222 signs enabled us to determine and tabulate the most informative ones (Table 1). Analysis of the values of the *t* criterion revealed that the greatest changes after the tests occurred in virtually all of the listed signs in the first group. The changes were less marked in the second and third groups.

Table 1. Changes in the most informative parameters

Parameter	Group					
	1		2		3	
	AOH					
	before	after	before	after	before	after
Girth, cm:						
abdomen	85.0	91.5*	90.1	93.1	89.0	92.7
neck	37.8	38.7*	39.6	39.5	39.0	39.4
chest	92.8	94.4	96.7	99.7	98.0	98.7
thigh	52.4	55.0*	56.9	59.9*	55.1	56.9
leg	37.1	36.0*	38.6	38.2	38.1	34.7
arm	29.9	31.1	31.5	32.6	31.2	31.7
Fat folds, mm						
on abdomen	17.1	27.5*	18.9	27.8**	19.0	24.8*
on thigh	10.5	17.5*	13.4	18.3*	10.8	16.4*
Tissue weight						
fatty, kg	10.8	14.4*	11.96	14.5*	12.7	13.1
fatty, %	14.4	18.5*	14.2	16.6*	15.5	16.0
muscle, kg	33.3	32.3	38.7	39.8	35.5	34.5
muscle, %	45.6	41.8**	46.4	45.8	45.3	43.6
Weight of segments, kg						
head	4.93	5.13*	5.1	5.4*	5.18	5.3
middle part of trunk	13.7	14.7*	14.6	15.5	13.7	14.4
thigh	10.0	10.9*	11.48	11.9	10.7	10.7
lower leg	3.07	3.104	3.56	3.48	3.28	3.2
total weight	73.38	77.68*	83.6	86.92	78.76	79.55

* $P < 0.05$
 ** $P < 0.001$

In all three groups, we found the same tendency of reliable increase in thickness of fat folds on the abdomen and thighs. There was a corresponding change in girth of the abdomen and thighs. However, the mass of the thighs increased with statistical reliability only in subjects of the first group.

The change in weight of adipose tissue was almost twice as significant in the first group as in the second, the muscle mass diminishing in the first group by 3.8%, i.e., by an average of 1 kg, which is 6 times more than in the second group and twice as much as in the third.

There was a reliable increase in mass of the middle part of the trunk, thighs, head and neck (with particular increase in that of the thighs) in the first group of subjects. In the second group, there was reliable increase only in mass of the head and neck. The girth of the lower leg diminished in all groups of subjects; however, this was reliable only in the first group, in spite of the fact that the cutaneous fat fold on the legs of subjects of this group increased. The lower leg mass changed insignificantly in all groups.

Table 2. Individual changes in parameters

Group	Mass, kg	Girth Δ, cm		Adipose folds Δ, mm			Mass Δ, kg			Tissue mass Δ, %	
		neck	abdom.	scap- ula	abdom.	leg	upper body	middle part of body	leg	fat	muscle
First											
O-ov	-2.0	+1.0	+5.5	+1.0	-1.0	+2.5	-0.2	0	0	+1.5	-3.27
P-ov	+3.60	+0.8	+2.0	-1.0	-8.0	+0.5	+1.4	-0.60	-0.23	+4.7	-3.7
G-ov	+9.57	+0.8	+10.7	+5.5	+17.0	+1.5	+3.44	-0.03	+6.86	-	-3.7
P-ov	+0.58	+1.5	+0.3	+2.0	+8.2	+1.0	-4.9	-2.93	0	+1.9	-3.2
A-ov	-6.27	+1.3	-8.5	+3.5	+13.5	+4.5	-0.3	+1.2	+4.5	+7.8	-6.4
K-ov	-3.76	0	+6.4	0	+16.0	+0.5	+0.6	+1.5	+0.03	+4.6	-3.2
Second											
M-ov	-0.65	-1.2	+3.0	0	+5.5	-0.5	-1.0	-0.4	0	+0.5	-0.8
P-ov	+7.08	+0.5	+5.0	+5.0	-8.5	-4.0	+0.8	-2.7	-0.24	+5.4	-1.4
G-yn	+4.92	+1.3	+4.7	+1.5	-9.0	-1.0	+1.6	-0.9	-0.08	+2.8	-1.5
G-ov	+6.46	+0.1	+5.0	+1.5	+13.5	+0.2	-0.47	+1.6	-0.155	+2.3	+1.1
A-yev	+4.335	-1.0	+4.5	+3.0	+11.0	+2.0	+0.75	+0.47	+0.15	+2.5	-1.1
D-ov	-2.1	-0.3	-3.0	-4.0	+6.0	-0.5	-0.5	-0.16	-0.25	+0.1	-1.6
Third											
S-ov	+1.17	+1.9	+3.5	+1.4	-1.0	+0.5	0	-0.24	-0.26	+1.3	-0.6
S-in	+7.5	+1.5	+14.0	+0.7	+12.5	+1.7	-0.2	-3.1	+0.1	+3.0	-0.8
G-in	+0.785	-1.5	+1.3	-0.2	-2.0	-0.6	-0.3	+1.7	-0.45	+0.5	+0.75
S-ko	-2.55	-1.1	-0.6	-9.5	-4.0	-3.5	-0.3	-0.34	-0.17	-2.7	-6.0
N-yev	-0.82	+1.0	+3.0	-2.5	+5.5	0	+1.1	+0.2	-0.38	+0.3	-1.6
M-yev	-1.35	+0.8	+1.0	-3.0	+12.0	-1.0	-2.0	-0.3	-0.14	+1.8	-1.6

On the basis of the obtained data it was assumed that there was redistribution of mass in the subjects after the study. The most marked changes occurred in the first group, and while the amount of adipose tissue increased mainly in the middle of the trunk and thighs, the amount of muscle tissue diminished in muscles responsible for maintaining a vertical position.

In order to confirm this hypothesis, we analyzed the individual changes in the most informative parameters of the subjects (Table 2). The fact of the matter is that, in the case of a small sample (6 people in each group), the arithmetic mean is a rough description of phenomena occurring in the subjects. It, so to speak, smooths out individual distinctions of a man's reaction to test factors. In Table 2, of greatest interest are the relatively greater changes in adipose and muscle tissues of individuals in the first group and, at the same time, the changes in different directions in these parameters of subjects in the other groups.

Analysis of changes in lower leg mass and size of cutaneous fat fold on the posterior surface of the crus indicates that when the mass of the crus exceeded the base value the adipose fold was enlarged. An analogous (and even more distinct) tendency is demonstrable with regard to the middle section of the trunk; in other words, there was redistribution of components in the mass of the segments, in the direction of an increase in fatty mass and decrease in muscle mass.

The uneven distribution of enlarged adipose mass is interesting. In all groups of subjects we observed a significant enlargement of the adipose fold on the abdomen, with substantially less change in subscapular folds. Evidently, the subjects'

position in bed (mainly supine) create conditions (compression of tissues, diminished blood flow, etc.) that prevent deposition of adipose mass in dorsal tissues.

Thus, the method we used enabled us to demonstrate the distribution of masses in the human body as a result of examination and alteration of masses of different parts of the body. The combination of this method and anthropometry enabled us to make a differentiated evaluation of the nature of distribution of adipose and muscle masses in the human body.

In all subjects, there was a significant increase in adipose mass of the trunk and thighs, and the most probable causes could be the following:

1) Inconsistency between qualitative and quantitative composition of food and energy expenditure. Unfortunately, in our study the diet was the same for all subjects and, of course, it had too many calories for the subjects in the first group, whose expenditure of energy was minimal and close to basal metabolism (about 1800-2000 kcal/day), and this led to deposition of fat in tissues. For subjects in the second and third groups, the caloric value was balanced but not the qualitative composition, i.e., there was excessive intake of carbohydrates (unlimited intake of bread when the appetite was good) and shortage of protein. The latter circumstance resulted in an unbalance between catabolic and anabolic processes in favor of the former. It also served as the cause of reduction of muscle mass in the second and third groups, since the deficiency of plastic material did not compensate for the breakdown of protein due to both hypokinesia itself and regular exercise.

2) Inadequate choice of both intensity and nature of exercises. The fact of the matter is that the subjects in the second group were not homogeneous with regard to physical conditioning (three presented a high level of prior conditioning and the others an average level), while the structure of the exercises and load were the same for all of them, due to the need to have a minimum number of variables for analysis. For this reason, the load was adequate for some subjects and corresponded to a moderate level, while for others it was small and was on the light or below average level. Analysis of heart rate (HR) recorded in the course of all of the exercising revealed that its mean value (with due consideration of exercise and intervals between it) did not exceed 120/min throughout the period of the study, while the mean maximum did not exceed 145/min. These figures correspond to moderately heavy exercise [work]. On the other hand, if we analyze the progress of exercising in the third group, we will be impressed by the fact that there was less deposition of fatty tissue in this group than in the others, although there was also a reliable enlargement of adipose folds on the abdomen and thighs, but the mass of adipose tissue (in all) increased insignificantly. These findings can be attributed to the fact that the exercises were very intensive during the last 3 weeks of the study, and the HR reached 160-180/min, and even 200/min in some subjects. Evidently, this intensity of exercise was instrumental in burning up fatty accumulations and eliminating signs of adiposity, intensification of outlay of plastic material that was not adequately replenished exogenously. Onset of protein deficiency affected loss of muscle mass in this group. This intensive exercise had a particularly adverse effect on one subject who lost about 4.5 kg muscle mass and about

Table 3. Dynamics of motor system status in the course of 182-day AQH (% of background values)

Parameter	50th day			90th day			135th day			1st day of RP			14th day of RP			30th day of RP		
	1**	2		1	2		1	2		1	2		1	2		1	2	
		3			3			3			3			3			3	
Strength																		
Femoral extensors	86*	96	93	76*	93	95	75*	92	91	70*	95	92	94	89	97	100	100	100
Crural	85*	103	88	78*	96	91	76*	93	86	81	81	90	93	82	88	97	94	94
Trunk	85*	97	83*	74*	94	86	70*	94	85*	61*	96	90	97	87	94	106	89	89
Femoral flexors	82*	96	100	84	90	90	80*	88	94	74*	104	90	94	94	90	98	98	98
Crural	96	105	95	80*	111	84	76*	111	89	84	115	84	111	105	96	122	110	110
Foot	88*	104	94	82*	101	93	75*	101	110	72*	98	96	105	105	114	114	122	122
Static endurance																		
Abdomen				36*	113	92	32*	129	85	21*	169	43*	146	97	105	137	125	125
Back				43*	76	58*	48*	73	57*	22*	85	45*	98	63*	88	97	98	98
Foot				53*	83	70*	64*	84	73*	28*	94	67	96	78	87	97	103	103
Dynamic endurance																		
Abdomen				40*	118	99	41*	137	109	27*	180	84	181	113	114	145	129	129
Back				70*	77	80	57*	82	78	43*	103	80	94	75	106	113	104	104
Lability of myoneural system																		
Thigh	58*	86	73*	60*	85	95	62*	90	93	58*	90	65*	89	93	92	106	111	111
Upper arm	78*	92	87	82*	97	87	80*	101	92	76*	92	80*	96	86	94	107	99	99
Lower leg girth	91*	95	93	90*	94	91	89*	92	88	90*	93	88*						

*p<0.05

**Groups

2 kg adipose mass, along with 2.5 kg loss of overall body mass (mass exceeded background data by 1.5-2.5 kg on the 50th-90th-135th days of the study), and body mass was not restored even on the 14th day of the re-adaptation period (RP). In another case, the loss of muscle mass was not as significant (about 1.5 kg); however, overall mass continued to decline in the RP. Thus, we see that there is some inconsistency between intensity of exercise and functional capabilities of the skeletomuscular system of a number of subjects in the third group. It must be noted that an equally intensive load at the final stage of the study elicited a perceptible and immediate effect on some functional parameters of the motor system, i.e., by the end of AOH there was equalization of parameters for the third and second groups, whereas at the intermediate stages (the 50th-90th-135th days) there was substantial deterioration of these parameters in subjects of the third group. However, this effect was transient. On the 14th day of the RP, in spite of the set of rehabilitation measures, there was significant decline of parameters of static endurance (back, foot) and strength (extensors of the lower leg and trunk, flexors of the lower leg and thigh) in the third group of subjects, whereas in the second group they consistently improved. By the 30th day of the RP, there was virtual restoration of functions, according to a number of parameters, in subjects of the first group.

Table 3 lists some data from our study of the status of the motor system.

Thus, our studies revealed that the γ -scanning method used for segments of the body in the proposed variant enabled us to gain an idea about the redistribution of masses in the human body as a result of 6-month hypokinesia and about the segments of the body that are the most susceptible to the influence of insufficient muscular activity. With this method, it was demonstrated how much influence the second variant of exercising during hypokinesia had on redistribution of masses, and the causes of flaws in organizing the exercise process were disclosed.

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CHEMICAL COMPOSITION OF MINERAL COMPONENT OF HUMAN VERTEBRAE AND CALCANEUS AFTER HYPOKINESIA

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[Article by A. I. Volozhin, I. Ye. Didenko and G. P. Stupakov, submitted 6 Nov 79]

[English abstract from source] Hypokinesia of 20-42 days led to a decrease of Ca content and increase of K and Na content in the mineral component of human vertebrae, the Mg and P content remaining unchanged. It is suggested that these changes resulted from shifts in ion metabolism on the surface of hydroxylapatite crystals as well as from increase in the content of calcium phosphate amorphous component. The hypokinesia did not cause chemical changes in the inorganic component of os calcis, probably, due to the low metabolic activity of its microstructures. After hypokinetic exposure the mineral density of vertebrae and os calcis did not differ from the control value, i.e. no osteoporosis was seen.

[Text] When man is kept on bed rest the removal of weight from the skeleton leads to development of osteoporosis in some parts (calcaneus), as indicated by the decreased amounts of minerals in bone tissue, as demonstrated by roentgenophotometric and photo absorptiometric methods [1, 2]. The distinctions of chemical composition of human bone tissue during long-term hypokinesia have not been investigated, for which reason we undertook this study.

Methods

We examined whole thoracic and lumbar vertebrae, as well as calcanei, from cadavers of 9 individuals who died at the age of 22 to 45 years. Data obtained from examination of bones of 4 individuals who died of accidental causes were used as the norm (control group). Another group consisted of 5 people who had been under treatment, with strict bed rest, for 20-42 days at therapeutic institutions in Moscow and who died of suddenly occurring complications (myocardial infarction, thrombosis of the pulmonary artery, edema of the lungs and edema of the brain). We isolated 3-6 thoracic and 3-4 lumbar vertebrae, and the calcaneus from the cadavers (in all, we examined 67 vertebrae and 9 calcanei), and removed all soft tissues from them.

We assayed the volume of minerals (mineralization) of bones by a method that was described previously [3]. The bones were ashed in a retort [muffle furnace] at a temperature of 700°C for 7 h. The ash of each vertebra and calcaneus was ground

separately in a porcelain mortar, and batches of 100-120 mg were prepared, then a flame photometer used, in our modification of the conventional method [4] to assay Na and K content; an atomic absorptiometer was used to measure Ca and Mg, and a spectrophotometer, using molybdenum ammonia, for assay of P.

The data were submitted to processing by methods of variation statistics.

We used the mean concentrations separately for thoracic and lumbar vertebrae for correlation analysis to evaluate the correlation between levels of the elements under study.

Results and Discussion

Bed rest did not lead to changes in mineralization of vertebrae and calcanei, as compared to the control group, i.e., there was no development of typical osteoporosis over the period in question.

Ca content constituted 35.0 to 38.7 g/100 g ash (see Table) in the vertebrae of the control group (overall data are listed for thoracic and lumbar vertebrae). Even less fluctuation was demonstrated in P content.

Mineral content of human vertebrae and calcanei (per 100 g ash) under normal conditions and following hypodynamia

Mineral	Vertebrae			Calcanei		
	control	hypo-dynamia	% of control	control	hypo-dynamia	% of control
Ca, g	36.72±0.56	34.46±0.53	93.8*	37.97±1.40	36.97±1.21	99.7
P, g	16.68±0.19	16.78±0.17	100.6	16.63±0.85	16.63±0.14	100.0
Mg, mg	502.7±5.8	488.9±5.73	97.2	515.9±8.98	502.6±13.74	97.4
Na, mg	511.9±6.37	601.0±7.83	117.4**	637.4±23.5	645.0±18.66	101.2
K, mg	24.25±1.19	42.60±4.18	183.2**	31.32±5.32	28.96±2.26	86.1

* $P < 0.01$ ** $P < 0.001$

There was about the same amount of Na and Mg in the mineral component of vertebrae of individuals in the control group, with relatively minor individual differences. The concentration of K fluctuated over a wider range, from 18.2 to 30.1 mg/100 g ash.

As to chemistry of the mineral component, the calcaneus had a higher K and Na content than vertebrae (by 20-30%; $P < 0.01$); the concentrations of Ca, P and Mg were about the same in the calcanei and vertebrae.

We demonstrated a highly reliable positive correlation between Na and K ($r = 0.83$) and a negative one between concentrations of K and Mg ($r = -0.70$) in control vertebrae and calcanei. Accordingly, there was a negative, but less marked correlation between Mg and Na ($r = -0.52$). These data serve as grounds to believe that there is synergism between Na and K, and antagonism between K and Mg in the kinetics of metabolism of these elements with crystalloids of hydroxylapatite.

There was a close negative correlation between Ca and Na ($r = -0.85$) and between Ca and K ($r = -0.87$) in the calcaneus of control individuals. In view of the higher Na and K levels in calcanei, as well as the results of correlation analysis, it can be concluded that these elements are elements of the hydroxylapatite structure.

The vertebrae of individuals in the second group revealed a lower than normal Ca content, in the presence of normal concentrations of P and Mg. Concurrently, we found an increase in concentration of Na and particularly K.

The decreased Ca content and Ca:P ratio with hypodynamia could have resulted from an increase in amorphous calcium phosphate content [5]. For example, it has been established that an increase in amount of crystalline phase of bone in ontogenesis is associated with a decrease of the amorphous phase with concurrent increase in molar Ca:P ratio [6].

On the whole, a less close correlation was found between Na and Ca content in the vertebrae of individuals who had been on bed rest, as well as between K and Na in the inorganic substance of bone tissue. This circumstance indirectly confirms the opinion that, during hypodynamia, there is an increase in amount of amorphous unstructured calcium phosphate in bone, since this compound, unlike hydroxylapatite, is not metabolized with other mineral ions.

The chemical composition of calcaneus ash and correlation between different elements in individuals who had maintained bed rest showed virtually no difference from the findings in the control group.

To sum up our findings, it can be concluded that there is a change in chemical composition of the mineral component of human vertebrae as a result of 20-40-day hypodynamia, which is manifested by a decline in Ca content and rise in K and Na levels, against the background of normal P and Mg content. The mechanism of these changes is not clear; however, there are grounds to believe that the lack of static load on the spine and change in composition of fluid surrounding the microcrystals affect the reactions of ion metabolism on the surface of hydroxylapatite, primarily Na and K. The decrease in value of Ca:P ratio is perhaps the result of an increased amount of amorphous phase of calcium phosphate in bone tissue.

The lack of such changes in the calcaneus in the absence of a weight load on the skeleton over the above-mentioned period is apparently attributable to less marked metabolic activity of its microstructures than in vertebrae.

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EFFECT OF REMAINING BRIEFLY IN ORTHOSTATIC AND ANTIORTHOSTATIC POSITIONS ON MAN'S TRACKING PERFORMANCE

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[Article by Yu. N. Taranenko, submitted 31 Oct 79]

[English abstract from source] The studies were performed using a special trainer made of a table allowing tilts in the frontal plane equipped with a potentiometric control stick and electron-ray indicator. The studies demonstrated that a 30-min exposure to orthostasis or antiorthostasis deteriorated significantly the tracking capacity. It is assumed that the changes were induced by hemodynamic effects due to body position changes.

[Text] In recent years there has been an appreciable increase in number of studies of the distinctions of operator performance during exposure to space flight factors, which is attributable to the increase in volume and complexity of the tasks put to cosmonauts [1, 2]. Studies have been made of operator performance with exposure to accelerations [3, 4], vestibular stimuli, noise [5], hypoxia [6], etc. Hemodynamic changes are among the factors that are constantly present during space flights, which have a substantial effect on the cosmonaut's condition [7]. The close correlation between redistribution of blood in the body and poorer orientation was confirmed by the results of studies involving the use of brief orthostatic factors or lower body negative pressure [8, 9]. Model studies with the use of hypokinesia also demonstrated distinct deterioration of accuracy of man's orientation in space [10].

In view of these data, as well as the fact that spatial orientation is one of the most important features on which operator performance is based, our objective here was to examine tracking under the influence of being in orthostatic and anti-orthostatic positions.

Methods

In this study we used a device to tilt a subject in the frontal plane [11]. In accordance with our objectives, this device was adapted for conducting the tests with the subject in standing position. We first immobilized the trunk, extremities (with the exception of the right hand) and head, then moved the operator to the required position. There was an instrument on the device to examine tracking performance, which consisted of a potentiometric control on the right arm rest of the table [device] and a cathode-ray indicator. The indicator was attached to

a bracket in front of the operator (at a distance of 350 mm) and moved with it when the turntable was tilted, the operator's field of vision being limited by the tube. A stationary guide line and color mark that moved at random were exhibited to the operator on the indicator screen. A random signal generator caused aperiodic movement of the light in both directions from the guide line at a specific frequency. An MN-7 analog computer was used to model the frame of reference of random signal parameters, object to be controlled, adder, frame of reference of parameters of operator work. The operator's task was to eliminate mismatch errors between the guide line and color mark by means of the control. The magnitude of error was evaluated in arbitrary units. The work cycle of compensatory tracking constituted 3 min, and it was performed with the operator in a stationary position.

We conducted four main (2 with the operator in orthostatic and 2 in antiorthostatic position) and three control series of studies. Each series consisted of three phases, with three work cycles of compensatory tracking in each phase. In the main series, where we used orthostatic and antiorthostatic positions, the operator was in the same position in the first and third phases (at an angle of 30° from the vertical plane or in horizontal position, 15 min in each phase). In the second phase, the operator was in vertical position (orthostasis) or at an angle of 120° from the vertical plane (antiorthostasis). This phase lasted 30 min. In the control series, the position of the operator in space remained unchanged for all three phases; it corresponded to the first and third phases of the main series. The choice of the first position, at an angle of 30° from the vertical plane (in the first 3 series of tests), was substantiated in a preceding study [9], in which it was demonstrated that it is expressly in this position that there is the most distinct manifestation of sensitivity to orthostatic factors according to orientation parameters. During the studies, the operator tilted to both the right and left of the vertical plane.

We conducted seven series of studies, in which the subject assumed the following positions:

Series I (main): 1st and 3d phases, body tilted 30° to the right from vertical; 2d phase, vertical position

Series II (control): 1st, 2d and 3d phases, body tilted 30° to the right from vertical

Series III (main): 1st and 3d phases, body tilted 30° to the left from vertical; 2d, vertical position

Series IV (main): 1st and 3d phases, horizontal body position on right side; 2d phase, body tilted 120° to the right of the vertical plane

Series V (control): 1st, 2d and 3d phases, horizontal position on right side

Series VI (main): 1st and 3d phases, horizontal position on left side; 2d phase, body tilted 120° from vertical plane

Series VII (control): 1st, 2d and 3d phases, horizontal position on left side.

Twelve subjects participated in these tests, and they had previously developed a stable skill in tracking on this equipment. We used the method of comparing growth

curves, plotted for three points (I, II, III), which reflect the magnitude of error in a single work cycle over one phase [12], to process the results.

Results and Discussion

The results of these studies (see Table) revealed that there was a distinct (statistically reliable) increase in operator error while performing the task of compensatory tracking (Figure 1) after spending 30 min in orthostatic position (series I). In the control series, where the orthostatic factor was not used, no difference was demonstrable between tracking quality in the first and third phases. Evidently, the fluctuations of error in this series over the entire test were random in nature. In series III, where the subject tilted to the left in the first and last phases, the orthostatic factor elicited a statistically reliable increase in error.

Effect of 30-min in orthostatic and antiorthostatic positions on quality of operator performance of compensatory tracking in first and third phases of test (in arbitrary units)

Time of Series	Phase of test					
	1			3		
	work cycle					
	I	II	III	I	II	III
I	30° (→)			30° (→)		
	115.1±7.3	115.6±7.8	115.1±8.9	121.0±9.5	127.2±10.5	123.4±10.3*
II	30° (→)			30° (→)		
	120.1±7.2	115.0±5.2	118.7±7.6	114.3±9.9	119.1±9.6	111.2±8.9
III	30° (←)			30° (←)		
	107.0±5.6	116.4±4.4	113.5±5.5	123.4±7.9	129.3±7.7	125.0±5.8*
IV	Horizontal (→)			Horizontal (→)		
	113.0±5.7	120.0±6.9	123.3±9.6	128.4±8.8	134.3±8.4	136.0±8.9*
V	Horizontal (→)			Horizontal (→)		
	118.4±5.2	119.9±5.5	120.3±5.9	111.7±5.6	121.6±6.2	117.5±5.9
VI	Horizontal (←)			Horizontal (←)		
	118.4±4.9	117.5±6.2	119.7±6.0	117.6±6.2	120.7±6.4	126.7±7.5
VII	Horizontal (←)			Horizontal (←)		
	118.0±7.2	123.4±6.7	127.2±7.5	127.8±8.4	127.3±8.9	127.6±6.2

Note: The arrows indicate tilting of the operator to the right (→) or left (←) from the vertical plane; the asterisk indicates a reliable difference in tracking quality when comparing the curves for the first and third periods.

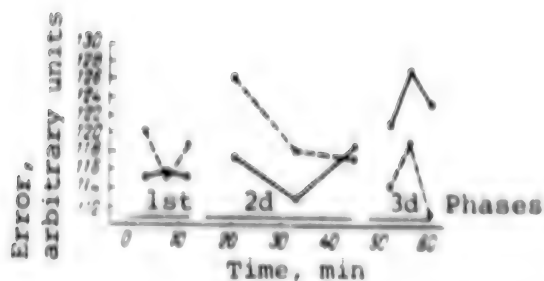


Figure 1.

Effect of brief stay in orthostatic position on quality of tracking performance. Here and in Figure 2: solid line refers to main series and dash line to control series of tests

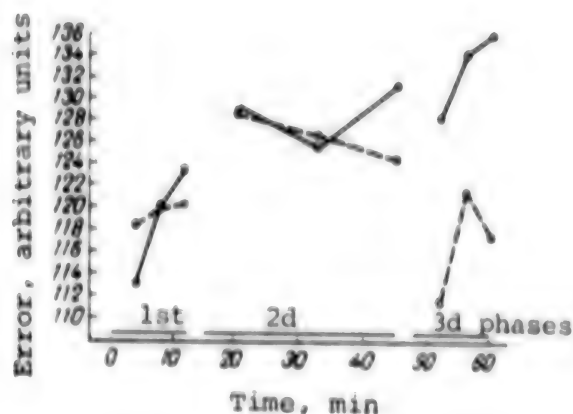


Figure 2.

Effect of brief stay in antiorthostatic position on operator's tracking performance

Similar findings were made in the series with antiorthostatic position, when the operator was on his right side (Figure 2). In this case, staying at an angle of 120° from the vertical led to reliable worsening of tracking accuracy when the operator returned to horizontal position in the third phase, as compared to the first. In the control series, where the subject remained on his right side throughout the test, these tracking errors coincided in the first and third phases. However, being in horizontal position evidently is not indifferent to operator performance. This is also indicated by the appreciable increase in tracking error in the control series, at the second phase.

In series VI, where the operator was submitted to antiorthostasis when on his left side, there was no appreciable change in error during the study. There was merely some tendency toward increased error. In the control test, with the operator in horizontal position, there was no difference in magnitude of error between the first and third phases.

Since the initial level of tracking performance of the group of operators was virtually the same in all series of studies, we compared the magnitude of error in series I and IV. This comparison revealed that there was more significant increase in error after the operator had been in antiorthostatic position.

In all of the series, before, after and during examinations, we recorded arterial blood pressure and heart rate. We failed to demonstrate any significant deviations of these parameters from base levels during the time the subjects spent in both the main and control positions.

Thus, our studies revealed that a 30-min stay by man (an operator) in orthostatic and antiorthostatic positions leads to a decrease of tracking accuracy. Our results coincide with the data in works that described changes similar in direction in operator performance under the influence of accelerations, G forces, noise, etc. As we know, these factors led to diminished operator efficiency due to premature development of mental and physical fatigue, emotional stress, vestibular decompensation, etc. Our experimental conditions did not elicit any appreciable stress reaction, as can be seen from the absence of appreciable deterioration of tracking performance when the operators were in orthostatic and antiorthostatic positions.

as well as stable pulse and arterial pressure throughout the test. All this enables us to expound the following hypothesis concerning the mechanisms of the demonstrated changes. As we know, the system of estimating the positions of distant objects is one of the variants of man's spatial orientation. Interaction between man and space includes orientation in relation to the earth's surface, visible objects, etc. Evidently, the different forms and, accordingly, levels of orientation are inter-related and influence one another. In particular, it can be assumed that a change in the system of body orientation, which were demonstrated previously, and errors in estimating the positions of symbolic objects exhibited to the individual while performing operator tasks are the result of impaired afferentation of mechanoreceptors of static zones during the 30-min stay in orthostatic and antiorthostatic positions.

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STATE OF PERIPHERAL BLOOD AS RELATED TO ALTERED DIET AND STRESS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
pp 48-51

[Article by M. V. Markaryan, submitted 14 Jan 80]

[English abstract from source] The effect of diets prepared for prolonged space flights and stress exposures on peripheral blood of 42 healthy male test subjects was studied. The morphology of peripheral blood remained essentially unaltered, when test subjects were given dehydrated diets (freshly prepared, stored for 2 years and exposed to proton irradiation at a dose of 24,000 rad) or Salyut-6 space diet. Stress effects brought about neutrophil leukocytosis and lymphopenia which could be prevented with dietary supplements.

[Text] A study was made of the effect of diets developed for long-term space flights and stress conditions on the state of peripheral blood.

Methods

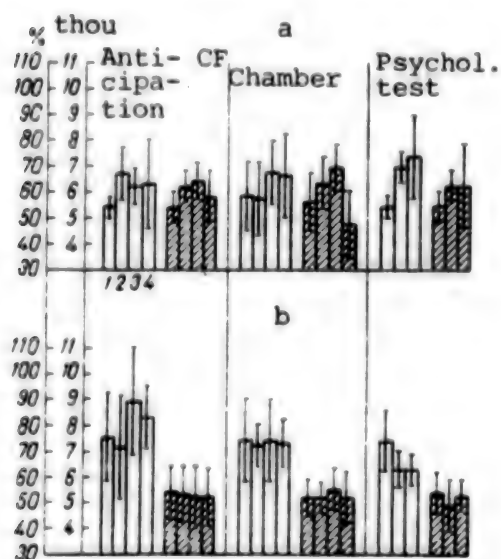
Seven studies were conducted on 42 healthy males ranging in age from 19 to 49 years. The general description of the studies and diets is given in Table 1. Peripheral blood was analyzed by the conventional methods used in clinical diagnostic laboratories [1]. The subjects kept on with their usual activities under medical supervision. The method for irradiating foods was described previously [2]. Neuro-emotional stress was induced by means of three models of stress situations: simulated ascent to 8000 m in a pressure chamber, anticipation of G forces on a centrifuge (CF) and performance of a psychological test. Corrective food supplements, which included various combinations of vitamins, minerals and glucose, were given to correct changes in metabolic processes and physiological functions, which were observed under the influence of the stress factors. The methods for producing neuroemotional stress and program for intake of food supplements were published previously [3].

Results and Discussion

The diets, which consisted entirely of dehydrated foods, as well as analogous diets that included foods stored for 2 years, or stored and exposed to 24,000 rad radiation (studies I-III) had no appreciable effect on peripheral blood of the subjects (Table 2). Their health status remained normal and alimentary status was satisfactory.

Table 1. General description of studies and diets

Study	Number of subj.	Time, days	Types of foods	Chemistry, g				Daily intake of Undevit multiple vitamins
I	6	60	Dehydrated by sublimation and heat drying	143	100,6	430	3290	1 lozenge
II	5	70	Dehydrated after 2-year storage	140	99	400	3130	1 "
III	5	70	Dehydrated after 2-year storage and exposed to 24,000 rad protons	140	99	400	3130	1 "
IV	6	35	Dehydrated and preserved [canned]	144	106	276	2708	2 "
V	10	60	Diet used for crews of Salyut-6 orbital station	141	95	345	2880	2 "
VI	5	60	Diet used for crews of Salyut-6 in the presence of stress factors	138	99	360	2970	2 "
VII	5	60	Salyut-6 diet, stress factors and intake of corrective food supplements	144	90	331	2790	2 "



Changes in leukocyte (white columns) and segmented nuclear (striped) content under the influence of stressors (a) and under analogous conditions against the background of food supplement intake (b)

- 1) background
- 2) before stress
- 3) after stress
- 4) 1 day after stress

The hematological parameters were also in the physiological range (see Table 2) on a diet consisting of preserved and dehydrated foods intended for crews participating in missions lasting 1 or more months.

Table 2. Hematological findings on the subjects (M±m)

Time of study, day	Hb, g%	Erythrocytes, million/mm ³	Color index	Reticulo- cytes, %	Thrombo- cytes, thou/mm ³
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Study I (n = 6)

Background	15.1±0.27	4.8±0.13	0.9±0.03	—	240±16
58th	15.5±0.26	5.1±0.07	0.9±0.03	—	230±23

Study II (n = 5)

Background	15.2±0.3	4.5±0.2	0.91±0.05	1±0.06	251±20
66th	14.3±0.5	4.3±0.2	0.97±0.4	0.9±0.1	200±10

Study III (n = 5)

Background	14.4±0.5	4.6±0.2	0.93±0.04	1±0.08	266±10
66th	13.3±0.5	4.5±0.3	0.9±0.03	1±0.09	273±20

Study IV (n = 6)

Background	14.2±0.3	4.5±1.0	0.9±0.08	0.9±0.01	279±7.2
34th	14.2±0.9	4.4±0.5	0.9±0.06	0.96±0.01	276±15.0

Study V (n = 10)

Background	15.9±0.4	5.9±0.28	0.87±0.05	0.8±0.045	262±4.1
58th	14±0.3*	5.1±0.03*	0.81±0.01	1±0.054*	280±11.4

Leuko- cytes/mm ³	Eosino- phils, %	Stab nucl. %	Segmented nucl., %	Lympho- cytes, %	Mono- cytes, %	ESR, mm/h
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Study I

Background	6600±648	3±0.22	1±0.16	58±2.5	30±3.0	6±1.0	5±0.66
58th	6100±650	3±0.37	1±0.3	56±2.7	34±2.8	6±0.6	6±1.0

Study II

Background	6100±700	2±0.3	1±0.3	67±1.2	26±1.5	5±0.9	4±0.6
66th	6300±700	2±0.6	2±0.6	59±3.8	31±3.4	6±1.1	5±0.9

Study III

Background	6600±600	1.8±0.2	1.2±0.2	56±1.9	34±2.3	6±0.5	7±3.1
66th	6300±400	4±1.4	1±0.2	55±0.6	34±1.2	6±1.4	8±1.2

Study IV

Background	5700±480	2.3±0.1	1.5±0.08	50±4.5	31±1.0	5±0.8	4.5±0.37
34th	5900±500	2.6±0.5	1.3±0.2	57±2.0	33±2.4	5.6±1.1	3.3±0.5

Study V

Background	6400±440	3±0.4	1±0.2	56±1.8	32±0.63	7±0.7	4±0.5
58th	7700±580	2.3±0.5	1±0.1	58±2.0	33±1.88	6±0.54	6±0.92

*Reliable differences between levels in background and experimental periods.

We also failed to demonstrate significant changes when using for 60 days the diet designed for the crews of Salyut-6 (see Table 2). Although comparative analysis revealed a statistically reliable decrease in hemoglobin concentration ($P<0.01$) and erythrocyte and reticulocyte content ($P<0.05$) on the 59th day, these changes were insignificant and all levels were within the physiological range.

With simulation of stress situations, the most marked changes were demonstrated in response to anticipation of CF (see Figure). Before CF and immediately after it we observed statistically significant increase in leukocyte ($P<0.01$) and segmented nuclear ($P<0.01$) content; there was a corresponding decrease in lymphocyte count, from 36 to 27% ($P<0.01$). After 24 h, the difference from background levels became unreliable. Simulation of ascent in pressure chamber elicited an increase in segmented neutrophils ($P<0.05$). There was also an appreciable decline of lymphocyte count after leaving the pressure chamber, from 36% in the background period to 20% ($P<0.01$); the relative lymphocyte content after leaving the pressure chamber constituted 11% in 1 subject. The changes in the leukogram were not associated with appreciable increase in leukocyte count ($P>0.05$). Segmented nuclear content was below the background level 1 day after use of this factor. We observed an increase in leukocytes ($P<0.001$) and segmented nuclears ($P<0.02$) before performance of the psychological test. Immediately after the test, these parameters remained on the same levels. We failed to demonstrate appreciable changes in erythrocytes or thrombocyte count in any of the studies.

The submitted data are consistent with the existing conceptions of the blood system's reaction to stress: neutrophil leukocytosis, lymphopenia and eosinopenia [4, 5]. None of the readings revealed the presence of eosinopenia [sic].

In the experiments with simulation of stress situations, in which we used the appropriate food supplements, no significant hematological changes were demonstrated (see Figure). Evidently, this could be attributed to the corrective effect of the food components, which prevented not only changes in the leukocyte formula, but a number of metabolic changes; they normalized secretion of digestive enzymes, elicited more marked productivity of mental function with less intensive vegetative manifestations.

Thus, when using diets intended for long-term space flights under ordinary living conditions, the morphological composition of peripheral blood does not undergo appreciable change. Stress situations elicit neutrophilic leukocytosis and lymphopenia. Corrective food supplements prevent occurrence of these changes.

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EFFICACY OF ALIMENTARY FACTORS IN THE RECOVERY PERIOD FOLLOWING LONG-TERM
ANTIORTHOSTATIC HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
pp 51-53

[Article by V. P. Bychkov, K. V. Smirnov and A. S. Ushakov, submitted 14 Jan 80]

[English abstract from source] Changes in metabolism and digestive function seen in 8 test subjects during 49-day head-down tilt returned to normal in those kept on supplemented diets (protein, polyunsaturated fatty acids and minerals) faster than in the untreated subjects. It is concluded that such supplements are beneficial for the recovery of health status after prolonged head-down tilt.

[Text] Our objective was to find effective methods of accelerating readaptation processes with the use of alimentary factors after individuals were submitted to antiorthostatic hypokinesia (head end of bed tilted down at an angle of -4°) for 46 days.

Methods

We tested the effect of antiorthostatic hypokinesia (AOH) on the alimentary status of 8 men ranging in age from 36 to 40 years. To determine the alimentary status, we studied the parameters of body weight, metabolism (protein, lipid, carbohydrate, vitamin, mineral) and digestive system function.

This study consisted of three periods: background (12 days), hypokinesia (49 days) and recovery (30 days). In the recovery period, the subjects of the experimental and control groups performed sets of exercises (burning up 836 kJ, or 200 kcal energy for the first 3 day, 2090 J, or 500 kcal, from the 4th day on).

The diet was strictly regulated and differentiated in accordance with the stages of the study (Table 1). The allowances consisted of freshly prepared unadulterated foods. During the hypokinetic period the diet contained fewer calories and lower amounts of the main nutrients than in the background period.

In the recovery period, the subjects were divided into two groups; the first, control group (3 people) was on the same diet as in the background period, while the main [experimental] group of subjects (5 men) were given the recovery period diet

(with food supplements). The alimentary rehabilitation measures involved supplemental intake of first-class animal protein (42 g), polyunsaturated fatty acids (8 g), mineral salts (1.6 g potassium, 300 mg calcium, 530 mg phosphorus and 60 mg magnesium). The supplements were supplied in natural products (beef, cottage cheese, dried apricots).

Table 1. Chemical composition of diets (analytical data)

Diet	Amounts, g				Caloric value, kJ (kcal)
	protein	fat	carbo-hydrates	ash	
Background	117.0	83.3	373.0	14.1	12013 (2874)
During hypokinesia	102.0	77.5	256.4	12.8	9154 (2190)
Recovery period:					
main group (1st-3d days + 200 kcal)	138.7	84.7	351.0	20.1	11683 (2795)
main group (4th-30th days + 500 kcal)	144.0	93.4	402.0	21.0	12987 (3107)
control group (1st-3d days + 200 kcal)	117.0	95.8	398.0	14.1	12553 (3003)
control group (4th-30th days + 500 kcal)	122.0	108.7	434.0	15.0	13752 (3290)

Table 2. Dynamics of subjects' body weight (kg)

Subject	Period					
	back-ground	hypo-kinesia, day		recovery, day		
		26	48	3	16	29
B-ov	58.3	58.5	58.5	59.2	61.0	61.5
V-ev	82.1	80.1	79.2	80.0	82.6	83.4
V-ko	78.2	75.2	74.3	75.0	78.0	78.0
V-lo	64.7	62.9	62.4	63.6	65.5	65.5
M-ov	85.4	82.9	81.7	82.6	82.1	82.0
S-iy	68.7	68.1	67.9	69.0	70.6	70.3
F-ov	62.4	61.6	61.7	63.0	64.0	65.4
F-ik	74.8	73.5	73.8	75.0	75.7	75.6
M.	71.8	70.3	69.9	70.9	72.4	72.7

We assayed total protein and its fractions, free amino acids, cholesterol total lipids, α - and β -lipoproteins and vitamin E in blood serum and plasma. Regulation of glycemia was evaluated from the results of testing blood sugar concentration using the glucose tolerance functional test.

We assayed total nitrogen, urea, ammonia, aminonitrogen, uric acid, creatinine, concentrations of vitamins C, B₁, B₂ and B₆ (4-pyridoxic acid) in 24-h urine.

We examined secretory, peristaltic and enzyme-secreting functions of the stomach, pancreas and bile-secreting function of the liver. We made balance studies of

several elements (nitrogen, calcium, phosphorus, magnesium, potassium, sodium and chlorine), and calculated assimilation of the main nutrients.

Results and Discussion

As shown by the results of our studies, there was a decrease in body weight (Table 2) and blood serum albumin concentration, with increase in levels of most free amino acids of blood plasma (Table 3), as well as concentration of cholesterol and β -lipoproteins in blood serum, with reduced glucose tolerance (in 6 out of 8 subjects), increased excretion of total nitrogen in urine (chiefly aminonitrogen), the level of excretion of which being related to body weight loss, in the subjects under the influence of AOH. There was increased excretion in urine of vitamins C, B₂ and 4-pyridoxic acid.

Table 3. Levels of free amino acids in subjects' blood plasma (mg/l)

Amino acids	Period						
	back-ground	hypokinesia (49 days)		recovery (28th day)			
		M $\pm$ m	P	1st group		2d group	
		M $\pm$ m	P	M $\pm$ m	P	M $\pm$ m	P
Isoleucine	0.86 $\pm$ 0.075	1.13 $\pm$ 0.054	<0.02	1.00 $\pm$ 0.189	>0.1	1.29 $\pm$ 0.097	<0.05
Leucine	1.83 $\pm$ 0.132	2.56 $\pm$ 0.270	<0.05	2.26 $\pm$ 0.160	<0.05	2.42 $\pm$ 0.156	<0.05
Lysine	2.96 $\pm$ 0.087	2.29 $\pm$ 0.175	<0.01	2.38 $\pm$ 0.188	>0.1	2.95 $\pm$ 0.502	>0.1
Phenylalanine	1.09 $\pm$ 0.106	1.55 $\pm$ 0.134	<0.02	1.53 $\pm$ 0.132	>0.05	1.28 $\pm$ 0.061	>0.1
Tryptophan	1.23 $\pm$ 0.058	1.49 $\pm$ 0.222	>0.1	1.06 $\pm$ 0.221	>0.1	0.96 $\pm$ 0.189	>0.1
Valine	2.35 $\pm$ 0.065	3.27 $\pm$ 0.101	<0.001	3.11 $\pm$ 0.257	>0.05	2.38 $\pm$ 0.159	<0.01
Methionine	0.40 $\pm$ 0.051	0.59 $\pm$ 0.015	<0.05	0.63 $\pm$ 0.153	>0.1	0.42 $\pm$ 0.016	>0.1
Aspartic acid	0.17 $\pm$ 0.024	0.24 $\pm$ 0.099	>0.1	0.35 $\pm$ 0.224	>0.05	0.27 $\pm$ 0.038	>0.1
Serine	1.52 $\pm$ 0.081	3.40 $\pm$ 0.225	<0.001	2.45 $\pm$ 0.258	<0.02	2.05 $\pm$ 0.269	>0.1
Glutamic acid	2.35 $\pm$ 0.116	3.43 $\pm$ 0.435	<0.05	7.85 $\pm$ 1.356	<0.001	9.48 $\pm$ 0.665	<0.001
Glycine	2.32 $\pm$ 0.118	2.60 $\pm$ 0.168	>0.05	2.35 $\pm$ 0.230	>0.1	2.20 $\pm$ 0.062	>0.1
Alanine	3.49 $\pm$ 0.093	4.26 $\pm$ 0.199	<0.01	4.49 $\pm$ 0.173	<0.001	4.96 $\pm$ 0.392	<0.001
Histidine	1.23 $\pm$ 0.072	1.27 $\pm$ 0.054	>0.1	1.40 $\pm$ 0.245	>0.1	1.29 $\pm$ 0.363	>0.1
Proline	2.66 $\pm$ 0.110	2.68 $\pm$ 0.091	>0.1	2.91 $\pm$ 0.649	>0.1	2.94 $\pm$ 0.330	>0.1
Arginine	1.75 $\pm$ 0.123	1.54 $\pm$ 0.044	>0.1	—	—	2.02 $\pm$ 0.185	>0.1
Tyrosine	0.95 $\pm$ 0.097	1.38 $\pm$ 0.134	<0.05	1.25 $\pm$ 0.081	>0.05	1.24 $\pm$ 0.068	>0.1
Cystine	0.45 $\pm$ 0.051	0.56 $\pm$ 0.093	>0.1	0.62 $\pm$ 0.067	>0.05	0.55 $\pm$ 0.091	>0.1

During bed rest there was a negative nitrogen balance. It constituted -2.7 g on the 9th-11th days of hypokinesia and dropped to -1.2 g by the 45th-46th day. These metabolic changes were due to prevalence of catabolic processes over anabolic ones during hypokinesia. We observed a negative balance of potassium, sodium and phosphorus in the hypokinetic period.

Alimentary rehabilitation measures, which were used on 5 subjects of the main group led to a marked positive nitrogen balance (+3.0 g), increase in albumin fraction of blood serum protein and faster termination of compensatory nitrogen retention, as compared to the control group.

There was faster normalization of the following parameters of digestive system function in the main group of subjects: pepsinogen content of urine; trypsin, amylase and invertase in duodenal contents; alkaline phosphatase in feces. The dynamics

of parameters of metabolism and digestive function in other subjects of the main group did not differ from those of the control group. During the recovery period, there was increased utilization of vitamins C, B₁ and B₆ in all subjects. Assimilation of protein, fat and carbohydrates was about the same in both groups throughout the study (90-93% for protein, 95-98% for fat and 96-98% for carbohydrates).

Thus, there were changes in the parameters of metabolism that we tested and weight loss under the influence of 49-day AOH, which was indicative of diminished anabolic processes and prevalence of catabolic ones under these conditions. Alimentary rehabilitation measures were associated with faster recovery of a number of the parameters under study, which was indicative of efficacy of these measures in restoring the functional state of the human body in the recovery period following long-term hypokinesia in antiorthostatic position.

EFFECT OF LEVEL OF MOTOR ACTIVITY ON AEROBIC EFFICIENCY OF HEALTHY MAN

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
pp 54-56

[Article by G. V. Machinskiy, submitted 28 Feb 80]

[English abstract from source] Bicycle ergometry studies in which 120 healthy male volunteers, aged 20-40, took part, showed that aerobic performance depended on their normal motor activity. In the test subjects, leading an active mode of life, maximum oxygen uptake and general work capacity were significantly higher than in those leading a sedentary mode of life. The data obtained give evidence that the people with diminished muscle activity should be recommended to do regular exercises in order to maintain aerobic performance.

[Text] The intensive development of cosmonautics, aviation and the navy has increased significantly physiologists' interest in studying the resistance of man to extreme factors. Data have been accumulated indicative of the adverse effect on the functional capabilities of healthy man of limited muscular activity, for example, during bed rest, which simulates some of the physiological effects of weightlessness [1-3].

The range of studies dealing with the effects of chronic insufficiency of exercise on various systems and functions is broadening. In particular, there are works indicative of a certain link between the increased incidence of cardiovascular disease and diminished physical exercise in man's routine activities [4-6].

At the same time, there has been a very limited number of studies directed at establishing a correlation between man's aerobic efficiency and level of his daily motor activity.

We submit here the results of bicycle ergometry studies of healthy individuals under the same geographic and social conditions, but who led different modes of life with regard to exercise.

Methods

We studied 120 healthy men ranging in age from 20 to 40 years who were divided into 2 groups, according to level of motor activity.

Parameters of aerobic efficiency of subjects in the first and second groups

Group	Age, yrs	VP, kg-m	HR/min	PV, l/min	RQ	Maximum oxygen uptake		Oxygen pulse ml/beat	OU, ml/l
						l/min	ml/kg/min		
I	20-30	11 101 ± 101.5 (10 000-15 000)	129.3 ± 2.07 (110-147)	110.1 ± 3.01 (85-132)	1.11 ± 0.012 (0.97-1.16)	3.61 ± 0.09 (3.04-4.15)	40.8 ± 1.22 (10.7-59.1)	19.1 ± 0.53 (16.6-21.7)	33.0 ± 0.78 (28.2-40.3)
	31-40	11 107 ± 191.2 (8 016-15 000)	125.1 ± 1.62 (117-136)	108.7 ± 3.78 (72-133)	1.09 ± 0.019 (0.97-1.20)	3.52 ± 0.06 (3.12-4.05)	45.4 ± 0.83 (19.9-57.2)	19.0 ± 0.39 (16.7-22.3)	32.9 ± 0.88 (27.7-40.0)
	Group mean	11 133 ± 104.6	127.2 ± 1.55	109.5 ± 2.17	1.10 ± 0.011	3.57 ± 0.05	47.2 ± 0.76	19.1 ± 0.31	32.9 ± 0.51
II	20-30	7930 ± 236.6 (5367-11 000)	126.1 ± 1.21 (117-136)	99.3 ± 1.83 (76-128)	1.10 ± 0.006 (1.02-1.18)	2.99 ± 0.05 (2.21-3.67)	41.4 ± 0.85 (29.5-52.8)	16.1 ± 0.30 (13.7-20.0)	30.3 ± 0.59 (11.2-37.2)
	31-40	8499 ± 155.5 (5933-10 000)	126.7 ± 1.39 (112-147)	97.2 ± 2.19 (64-127)	1.12 ± 0.011 (0.96-1.26)	3.02 ± 0.04 (2.40-3.63)	39.2 ± 0.50 (32.7-47.0)	16.2 ± 0.22 (12.8-19.0)	31.6 ± 0.77 (23.6-45.6)
	Group mean	8215 ± 146.7	126.4 ± 0.90	98.3 ± 1.44	1.11 ± 0.007	3.00 ± 0.03	40.0 ± 0.52	16.2 ± 0.19	30.6 ± 0.55

The first group consisted of 37 subjects (19 20-30 years old and 18 31-40 years) who had exercised regularly for the last 2-2.5 years (for 60-90 min 2-3 times a week) chiefly to develop endurance. The second group consisted of 83 men (40 were 20-30 years old and 43 were 31-40) who did not exercise regularly and led an inactive, mainly sedentary life.

We used the test involving a physical load that was progressively increased to the maximum on a bicycle ergometer to test aerobic efficiency.

After warm-up exercises, the subjects pedaled on the bicycle ergometer at a rate of 60-70 r/min. The load, which constituted 600 kg-m in the 1st minute, was increased by 200 kg-m every min up to the individually tolerated limit, i.e., as long as the subject was able to maintain the specified pedaling rate.

We recorded the pedaling time, heart rate (HR) by means of an electrocardiography, O₂ uptake and CO₂ output on an automatic gas analyzer and pulmonary ventilation (PV) with a dry gas counter. We calculated several parameters characterizing man's aerobic efficiency.

Results and Discussion

The group averages for age, height and weight were similar for both groups of subjects, while differences between them were statistically unreliable. At the same time, analysis of the results of the bicycle ergometer tests revealed that overall physical fitness and functional capabilities of the cardiorespiratory system differed appreciably in the subjects.

The Table lists parameters of aerobic efficiency for subjects in the compared groups. The first group of subjects was able to pedal on the ergometer for a longer time, for which reason the volume of their performance (VP) was an average of 26.1% ($P < 0.001$) greater than in the second group. HR and respiratory quotient (RQ) reached virtually the same levels in both groups at

the end of the pedaling, which was indicative of equal strain on the cardiorespiratory system. In most cases, pedaling stopped because of severe fatigue of the femoral extensor, which reached the point of severe pain in some subjects. A few men complained of marked general fatigue. No differences were demonstrable in incidence of these symptoms in the two groups, and this is consistent with the results of previous studies, in which it was found that local fatigue of the femoral quadriceps was the most frequent cause of discontinuing work on the ergometer in healthy young subjects, and dyspnea was the cause in elderly people with some age-related changes in the cardiovascular system [5, 7].

In subjects of the first group, maximum PV and coefficient of oxygen utilization (OU), which characterizes the efficiency of ventilation, were an average of 10.3 ($P<0.01$) and 7.0% ($P<0.05$) higher than in the second group.

Maximum oxygen uptake, which is the integral parameter of cardiorespiratory capacity, was an average of 16.0% higher ($P<0.001$), while the amount thereof per kg body weight was 15.3% greater ($P<0.001$) in the physically more active subjects than in the less active ones.

Oxygen pulse, which shows the amount of O_2 utilized by the body per cardiac cycle, was an average of 15.2% higher in representatives of the first group ($P<0.001$) than the second.

The values we obtained for the subjects' physiological parameters coincided with the results of researchers who used analogous methods to study aerobic efficiency of healthy, physically conditioned [8-9] and unconditioned [10] men in comparable age groups.

Studies of the age-related differences within groups in levels of the parameters under study revealed that only maximum oxygen uptake per kg weight was higher in the 20-30-year old men than in those 31-40 years of age. Intragroup differences in other cardiorespiratory parameters were less marked or virtually absent (see Table). The more marked difference in maximum oxygen output per kg weight that was found in the first group can apparently be related to the fact that with physical training aerobic efficiency increases more in young people.

The parameters of aerobic efficiency were better in the men of the first group who were 31-40 years old than in those of the second group who were 20-30 years old. For example, in the physically active men in the older group, maximum oxygen output, performance volume and oxygen pulse were an average of 15, 29 and 15% higher than in younger but inactive subjects.

Thus, as a result of the bicycle ergometer studies, substantial differences were demonstrated in parameters of aerobic efficiency, which depend primarily on the level of regular exercise, rather than age. Individuals who led a physically more active life presented higher parameters of overall physical fitness and functional capabilities of the cardiorespiratory system than subjects who are chronically inactive.

Studies conducted on healthy men revealed that, under conditions of strict bed rest, the parameters of aerobic efficiency begin to decline within 2 weeks [11]. At the same time, even with 6-month bed rest, a rationally planned set of preventive measures, one of the chief elements of which is cyclic exercise, can maintain man's aerobic efficiency on the required level [12].

The submitted data enable us to conclude that it is desirable to use exercises that develop endurance in order to preserve the functional capabilities of the cardiorespiratory system of individuals who experience hypokinesia. Under conditions of limited living space, widespread and effective exercising equipment can be used for this purpose, such as bicycle ergometers or treadmills.

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REGIONAL ANALGESIA BY CONDUCTION ANESTHESIA AND REFLEX THERAPY IN THE ACUTE RECOVERY PERIOD FOLLOWING ANTIORTHOSTATIC HYPOKINESIA

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[Article by L. L. Stazhadze, A. V. Vabishchevich, V. N. Tsibulyak, G. V. Chubarov, A. A. Titov, M. N. Avakyan, Zh. M. Kudryashova, V. V. Lenskiy and V. V. Bogomolov, submitted 25 Feb 80]

[English abstract from source] After 7-day head-down tilt at -8° six healthy male test subjects were exposed to leg anesthesia achieved by peridural anesthesia (3 subjects) and electroauriculoacuanalgesia (3 subjects), with circulation parameters being monitored. The anesthetic effect was not accompanied by significant changes in hemodynamics or homeostasis.

[Text] The constant tendency toward increased volume and complexity of special work done in orbit increases the risk of trauma to different parts of the body (dislocation, fracture, burn, etc.). In such situations appropriate analgesia may be required to alleviate pain and prevent shock reactions [1, 2]. However, the functional distinctions of the body during long-term weightlessness make it necessary to choose and use methods of controlling pain that would not themselves cause any additional and appreciable destabilization of systems that regulate homeostasis, while they provide adequate and prolonged nociceptive blocking.

We tested here two means of analgesia: peridural anesthesia (PA) and electroauricular analgesia (EAA).

Methods

This study was conducted on 6 essentially healthy men ranging in age from 26 to 38 years after 7 days of antiorthostatic hypokinesia in supine position with a tilt of -8° . The first group consisted of three subjects to whom 2% lidocaine was injected in divided doses in the peridural space at the level of the 2d-3d lumbar vertebrae [3, 4] to a total of 3.55-3.95 mg/kg body weight in order to rule out nociceptive sensitivity in the lower limbs; to anesthetize the right limb of the second group of three men, we inserted steel needles into biologically active points of both conchae and submitted them to electric pulsed stimulation from an Elita-4-Elektronika instrument through the inserted needles [5]. We used the shen'-men' points, for the sympathetic and lower extremity on the right ear and the thyroid and lung points on the left. The delivered current constituted

200 μ A, at a frequency of 12 Hz, with pulse duration of 0.5 ms, duration of train ("pack") of pulses was 5 s, and there were 1-s intervals between trains; trains of negative trapezoid pulses were delivered to the acupuncture points with 50 μ s anterior and posterior fronts. Electrostimulation lasted 60 min and aftereffect analgesia for up to 90 min.

We assessed the influence of these anesthetic methods on monosynaptic transmission in the spinal cord by the method of electroneuromyography, with recording of parameters of H and M responses and calculation of the ratio between them [6, 7].

Before, during induction and maximum effect of anesthesia, we examined the main parameters of central hemodynamics by catheterizing the aorta and superior vena cava, then calculated the circulatory parameters on a computer. The level of placement of catheters in the aorta and vena cava was monitored with a television-x-ray unit. The blood pressure curves were recorded with miniaturized P-37 piezosensors on a polygraph, with oscilloscope and industrial magnetograph. Blood pressure curves were analyzed by means of an electronic computer system, which consisted of an MN-18 analog computer and high-speed Elektronika-100 I computer. We examined regional hemodynamics. A PEO-64 videoscope ["vizuskop"] was used to measure the caliber of retinal vessels. Concurrently, we determined acid-base equilibrium and gas tension in samples of arterial, venous and capillary blood.

Results and Discussion

On electroneuromyograms, PA was associated with consistent changes in parameters of evoked potentials (Table 1): the amplitude of the H reflex diminished by a mean of 25%, the thresholds of H and M responses rose, there was a decrease in number of functional motor units of the myoneural system and almost 50% decrease in ratio between maximum amplitudes of H and M responses.

The caliber of central retinal veins (CRV) increased by 7%, the caliber of the central retinal artery (CRA) decreased by 5% and pressure in the central retinal artery increased by 5%. The pressure elevation in the central retinal artery (CRA) against the background of diminished vascular tonus can be interpreted as a compensatory reaction to maintain normal blood flow in the system of the internal carotid artery.

The changes in central circulation (Table 2) were quite moderate. We were only impressed by the average 7% decrease in stroke volume of the left ventricle with diminished rate of ejection of blood into the aorta and 10% increase in left ventricular function.

However, there were some variations of dynamics of the parameters depending on the dose of anesthetic injected in the peridural space. After giving 3.55 mg/kg lidocaine total peripheral resistance increased by 28%, stroke ejection by the left ventricle diminished by 16% and minute volume by 14%. Central venous pressure rose from 4.8 to 7.2 mm Hg, pulse arterial pressure equaled 45 mm Hg.

Administration of 3.75 mg/kg lidocaine was associated with 16% decrease in total peripheral resistance, 3% increase in stroke volume and 9% decrease in minute volume. Central venous pressure dropped from 12.5 to 6 mm Hg, while pulsed arterial pressure constituted 55 mm Hg.

Table 1. Electroneuromyographic study of effects of PA and EAA, M²m

Condi- tions	Threshold, mA		Amplitude, μ V		MU	$\frac{H_{max}}{M_{max}} \times 100\%$	N reflex		M response	
	H	M	U_{max}	M_{max}			latency period, ms	duration, ms	latency period, ms	duration, ms
PA	Before anesth.	8.8 ± 0.9	7.0 ± 0.1	7.0 ± 0.1	15.0 ± 10.1	11.8 ± 18.05	18.0 ± 8.01	1.7 ± 2.01	5.18 ± 1.22	21.19 ± 7.96
	During anesth.	10.0 ± 0.9	7.0 ± 0.1	7.0 ± 0.1	17.0 ± 12.02	25.6 ± 19.05	10.77 ± 5.11	13.11 ± 7.26	1.50 ± 0.47	24.54 ± 7.63
EAA	Before	5.7 ± 0.7	10.70 ± 1.09	10.500 ± 0.911	11.0 ± 9.18	16.84 ± 15.19	15.97 ± 2.86	13.96 ± 2.97	6.18 ± 0.81	17.66 ± 2.69
	During	5.8 ± 0.7	8.70 ± 0.31	7.100 ± 0.100	22.2 ± 70.17	10.49 ± 7.27	38.9 ± 4.54	17.36 ± 1.15	7.51 ± 1.24	20.30 ± 3.14

Key: H) thresholds of H reflexes M) thresholds of M responses MU) motor units

Table 2. Hemodynamic changes under the influence of anesthesia, M²m

Condi- tions	AP _{syst.}		AP _{diast.}		AP _{pulse}		HR/ min	MV, %	SV, %	TPR, %	V unit/s	LVF, %	CVP _m mm Hg	T _{per} , s	T _{syst.} , s	T _{diast.} , s
	mm Hg	mm Hg	mm Hg	mm Hg	mm Hg	mm Hg										
PA	Before	110 ± 6.10	99 ± 5.46	76 ± 7.11	52 ± 10.08	63 ± 7.94	100 ± 0	100 ± 0	100 ± 0	100 ± 0	57 ± 1.20	100 ± 0	9.5 ± 3.23	0.8 ± 0.02	0.79 ± 0.05	0.47 ± 0.03
	During anesth.	108 ± 2.57	102 ± 7.13	81 ± 10.08	45 ± 8.83	68 ± 10.08	93 ± 7.94	99 ± 14.5	99 ± 14.5	99 ± 14.5	4000 ± 420	110 ± 22.27	7.2 ± 11.64	0.89 ± 0.15	0.79 ± 0.01	0.47 ± 0.04
EAA	Before	121 ± 25.21	101 ± 25.63	86 ± 21.37	17 ± 1.20	81 ± 16.81	100 ± 0	100 ± 0	100 ± 0	100 ± 0	4000 ± 0	100 ± 0	6.5 ± 1.51	0.8 ± 0.13	0.79 ± 0.02	0.51 ± 0.07
	During	120 ± 23.54	99 ± 24.37	81 ± 21.95	19 ± 0.84	80 ± 9.34	91 ± 2.10	115 ± 1.36	91 ± 2.10	115 ± 1.36	4500 ± 420	87 ± 1.44	5.8 ± 5.00	0.80 ± 0.08	0.78 ± 0.01	0.51 ± 0.07

Key: HR) heart rate V) velocity
 MV) minute volume of heart LVF) left ventricular function
 SV) stroke volume of heart VCP_m) mean central venous pressure
 TPR) total peripheral resist.
 T_{per}) period of cardiac contraction
 T_{syst}) period of systole
 T_{diast}) period of diastole

A dosage of 3.95 mg/kg also elicited a decrease in total peripheral resistance (TPR), by 14%. However, stroke volume (SV) diminished by 9% and minute ejection increased by 26% due to marked tachycardia (126/min). Central venous pressure remained quite high (10.0 mm Hg, versus 11.3 mm initially), and pulsed arterial pressure constituted 34 mm Hg.

Electroneuromyography 30 min after the start of EAA revealed objective signs of depression of excitability of spinal motoneurons. This was manifested by elevation of thresholds of N and M responses by an average of 58 and 28%, respectively. The amplitude of the H reflex decreased by 56% and that of the M response by 30%. There was a 29% decrease in number of functional motor units, while the ratio of maximum amplitude of H reflex to M response decreased by 38% (see Table 1).

PCRA dropped by 7%, CRA did not change, CRV increased by 8%, which was indicative of some decrease in vascular tonus due to autonomic regulation.

There were no appreciable changes in parameters of central hemodynamics (see Table 2). We should, however, mention a 13% increase in TPR, faster ejection of blood into the aorta and 13% decrease in left ventricular output. Central venous pressure underwent virtually no change.

PA, which does not have a direct effect on higher nervous activity, elicited a stable and prolonged analgesic effect with relaxation of striate muscles in the corresponding part of the body. Consciousness and adequate spontaneous respiration were retained. Arterial hypotension, a 10-30 mm Hg drop of arterial pressure without change in pulsed pressure is considered to be one of the distinctions of peridural anesthesia; this drop is elicited by the dosage and level of anesthesia, on the one hand, and state of homeostasis and changes therein during surgical intervention, on the other. When there is an excessively deep sympathetic block, peripheral vasodilation is associated with an appreciable decline of venous return, pressure drop in the venae cavae and right atrium, and diminished cardiac output. A change in activity of the cardiovascular system, which is based on dysregulation of vascular tonus and diminished circulating blood volume against the background of general dehydration [8], is one of the consequences of weightlessness and its ground-based model, antiorthostatic hypokinesia. The results of the studies indicate that the doses of anesthetics we used, which induced adequate regional anesthesia, had a moderate influence on hemodynamic parameters. Nevertheless, we demonstrated some differences in dynamics of vascular tonus as a function of dosage of lidocaine. Thus, with lidocaine in a dosage of 3.95 mg/kg, we observed somewhat more marked vasodilatation and higher pulse rate than with doses of 3.55 and 3.75 mg/kg, with retention of parameters of cardiac output on a satisfactory level.

EAA created a block in monosympathetic transmission of stimuli on the corresponding level of the spinal cord which, according to electroneuromyographic findings, was even deeper than with PA. The stronger depression of afferent impulsation with EAA was consistent with the more effective analgesia in the "target" zone, i.e., in the selected part of the body. Our data are not in contradiction with the comparative clinical evaluation of these methods of analgesia, which was published in recent years. In particular, V. A. Mikhel'son, who compared the analgesic effects of acupuncture and trimecaine PA on children, reported that their efficacy was the same. There was also less inhibition of patients during acupuncture anesthesia [9].

Another distinction of EAA is that there is relatively high stability of aortic blood flow and hemodynamics as a whole. This feature of acupuncture is used with success in surgery at the present time [10]. Evidently, it is partially related to stable sympathetic stimulation, as a result of simultaneous effects on the selected group of biologically active points on the conchae. References have been made in the literature to results of studies that are important to substantiation of the mechanism of acupuncture analgesia, with indication of the lack of negative inotropic effects of EAA [11, 12]. The EAA method makes it possible to use acupuncture for both analgesic purposes and general fortification of the body, depending on the patient's condition. In this respect, acupuncture is close to so-called ideal anesthesia with regard to its potential capabilities.

The analgesia methods tested here are rather simple to use and do not require complicated equipment. Our findings are indicative of their high specific efficacy and feasibility in clinical space medicine during space missions and in the immediate postflight period.

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ACCELERATIONS AFFECTING MAN IN STORMY WEATHER

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pp 61-62

[Article by V. N. Barnatskiy, A. T. Poleshchuk, A. A. Shipov and V. A. Babushkin,
submitted 2 Jan 80]

[English abstract from source] The paper describes accelerations affecting men working aboard the ship of 22,000 tons displacement in stormy weather.

[Text] Studies of the last few decades established that the prime cause of motion seasickness (seasickness, air sickness and transport sickness) is long-term exposure of the vestibular system to linear or angular accelerations that change in direction [1]. The speed of onset of this sickness is largely determined by the time and amplitude characteristics of the vestibular stimulus. For this reason it is of great theoretical and practical interest to record and analyze accelerations that occur in transportation systems that man uses in his work.

We submit here the characteristics of accelerations that occur during violent and harsh storms,* to which man is exposed aboard ships.

Methods

We conducted our studies on the Atlantic Ocean and North Sea in January and February 1967 and 1977, aboard a base vessel of 22,000 tons displacement.

The ship's accelerations were recorded with inertial electrical VIA-6M sensors attached to the top deck 3 m away from the central longitudinal, vertical (diametric) plane of the ship, 25 m from the central transverse vertical plane (maximum midsection). We secured gyroscopic list indicators in the same place.

We recorded accelerations in the bow-stern, side to side directions, in the direction of the gravity vertical, as well as the angles of list during rolling and pitching. We recorded linear accelerations and list angles 4 times a day, for 5 min at a time, using a K2-12 loop oscillograph. The angular accelerations that occurred during listing were calculated from the tracings of heel angles.

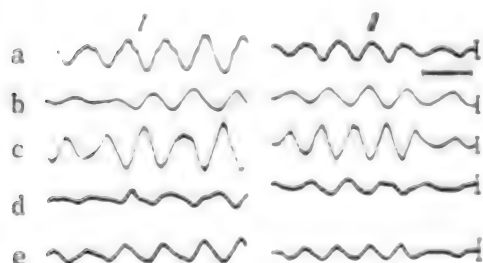
*In accordance with the classification adopted in maritime tables.

Results and Discussion

The Figure illustrates typical examples of tracings of angles of heel and linear accelerations during a violent and severe storm, with the ship moving with the "head to the wave." The fact of the matter is that when a ship moves at an angle or parallel to a wave ("broadside to the wave"), there is a decrease in pitching but marked increase in rolling. For this reason, in a heavy storm ships are usually held strictly in the position of "head to the wave," which diminishes appreciably rolling, with virtually no change in heaving.

Analysis of numerous tracings revealed that when the ship moves with the "head to the wave" during a heavy storm maximum accelerations in the direction of the gravity vertical constituted a mean of 0.22 G, and the period of vertical movements of the ship was close to 10 s. Maximum accelerations in the side-to-side and prow-to-stern direction constituted a mean of 0.07 G. Under these conditions, we established the following characteristics of the ship's rolling: period 11 s; maximum amplitude of heeling 2.4° , maximum angular acceleration $3^\circ/\text{s}^2$. When the ship moved with the "head to the wave" the period of pitching constituted 8 s, amplitude of heel was 4.8° and angular acceleration was $1.0^\circ/\text{s}^2$. The coefficient of variation of accelerations and angles of heel during heavy storms reached 93% in a number of cases, (especially at the start of a storm).

It must be noted that at the start of development of a storm, as well as during it, when the course was altered and the ship had to be "broadside to the wave," the angle of heel of rolling increased to 20° , angular accelerations to $30^\circ/\text{s}^2$ and side-to-side accelerations to 0.18-0.2 G.



Example of tracings of angles of heel and linear accelerations during storm

I) heavy storm, condition of sea rated as 9, wind force 12 (18 Jan 70)

II) severe storm, condition of sea 7, wind force 9-10 (21 Jan 70)

a,b) angles of heel of pitching and rolling, respectively

c,d,e) accelerations in directions of gravity vertical, side-to-side and bow-stern (in "d" units)

Calibration in a and b, 6° , in c, d, e, 0.1 G; time scale 10 s

Thus, when a man is aboard ship during a storm, he is subjected to linear and angular accelerations that change constantly in magnitude and direction. The characteristics of accelerations are determined by the condition of the water's surface, direction and force of wind, position of the ship, its displacement and design. When the ship moves "broadside to waves" the highest absolute values are referable to the components of linear accelerations in the direction of the gravity vertical and side-to-side, as well as angular accelerations of rolling. The occurring accelerations are many times greater than the threshold levels for stimulation of the vestibular system: 0.0003-0.07 G for otolith reactions and $0.035-8.2^\circ/\text{s}^2$ for reactions of semicircular canals [2]. In addition to rise in absolute magnitude of accelerations during storms, there is also increase in their variability [3].

When a man moves on the ship while it is pitching or rolling it leads to appearance of Coriolis accelerations, while any rotating movements lead to precession accelerations [4]. As shown by estimates, The Coriolis accelerations do not exceed 0.08 G, even when walking rapidly (1.6 m/s) and at maximum velocity of rolling (50°/s), i.e., lower than the maximum linear accelerations of the ship itself by a factor of 10. Precession accelerations appear mainly when the head is turned. The magnitude and direction of precession acceleration are determined by the vector product of angular velocities of ship tossing and head turning. The maximum rate of head turns is $840 \pm 270^\circ/\text{s}$ [5]. Consequently, the magnitude of precession accelerations could be greater by a factor of 10^2 than the maximum recorded angular accelerations of the ship.

Thus, when a man moves and performs his work in a storm situation, when the ship is moving at an angle or "broadside to the wave," the main etiological factor of seasickness is the effect of supraliminal linear accelerations differing in signs (primarily in the direction of the gravity vertical) and linear (precession) accelerations.

When the ship's course is held strictly heading into the waves and angular accelerations diminish appreciably, the chief pathogenetic factor in onset of seasickness is the effect on the vestibular system of linear accelerations of variable sign in the direction of the gravity vertical. In this case, seasickness develops more slowly than with a combination of angular and linear accelerations when moving at an angle to the waves [6]. It should be noted that under the conditions we studied, the period (frequency) of heaving was rather stable. As shown in [7], with a constant frequency of heaving the number of victims of motion sickness increases with increase in maximum acceleration. Hence it can be concluded that, as a storm develops, even when the ship is held strictly "head into the wave," the incidence of seasickness increases.

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STUDY OF HUMAN VESTIBULAR REACTIONS TO SIMULATED PERIODIC SHIP ROLLING

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
pp 63-66

[Article by V. M. Gusev, T. A. Salimova and V. A. Kislyakov, submitted 24 Apr 80]

[English abstract from source] Reactions of the semicircular canals to periodic effects of the ship rolling type have been studied using a mathematical model. The data obtained give evidence that during the above effects linear combinations of reactions of all semicircular canals may describe changes in the angular velocity of man's movements in an absolute (static) space. Besides, the common segment of the vertical semicircular canals (the common limb) allows a more accurate description of time changes in angular velocity. The mathematical model has demonstrated the dependence of absolute angular velocity as approximated by the semicircular canals upon head orientation as related to the body. In addition to general discussions about rolling effects on the semicircular canals, the paper presents calculations of such reactions as applied to a specific object, i.e. a medium-size trawler.

[Text] It was previously shown that the reactions of the hydromechanical system of the semicircular canals of the vestibular system at the early stage of exposure to dynamic perturbances can yield a rather exact estimate of the vector of angular velocity of a biological object in absolute (static) space. At the same time, we know nothing about the quality of such an estimate for the established reactions of the canals' hydromechanical system to prolonged periodic perturbations of the ship rolling type that are frequently encountered in real life.

In this work, using a mathematical model executed in the form of a computer program, we studied the reactions of the semicircular canal system to periodic oscillations.

Description of model of exogenous factors: When analyzing the processes in the labyrinth, we disregard the advancing movements of a ship's center of gravity associated with actual rolling. We link the start of the absolute system of coordinates x_0, y_0, z_0 to the ship's center of gravity (Figure 1) and direct this system of coordinates in such a manner that axis x_0 coincides with the local vertical and axis y_0 lies in the centerline plane of the ship and is directed toward the prow. In simplified form, ship rolling is the rotation of a system of coordinates x_1, y_1, z_1 that is rigidly fixed to the ship's hull in relation to center O over Eulerian angles ϕ and θ , where ϕ and θ are the angles of pitching and rolling, respectively.

$$\begin{aligned}
\hat{n}_{aa} &= -\hat{i} \\
\hat{n}_{ca} &= \frac{V\sqrt{2}}{2} (\cos \alpha - \sin \alpha) \hat{k} - \\
&\quad - \frac{V\sqrt{2}}{2} (\cos \alpha + \sin \alpha) \hat{j} \\
\hat{n}_{\phi a} &= -\frac{V\sqrt{2}}{2} (\cos \alpha + \sin \alpha) \hat{k} - \\
&\quad - \frac{V\sqrt{2}}{2} (\cos \alpha - \sin \alpha) \hat{j} \\
\hat{n}_{aa} &= \hat{i} \\
\hat{n}_{ca} &= \frac{V\sqrt{2}}{2} (\cos \alpha + \sin \alpha) \hat{k} + \\
&\quad + \frac{V\sqrt{2}}{2} (\cos \alpha + \sin \alpha) \hat{j} \\
\hat{n}_{\phi a} &= -\frac{V\sqrt{2}}{2} (\cos \alpha - \sin \alpha) \hat{k} + \\
&\quad + \frac{V\sqrt{2}}{2} (\cos \alpha + \sin \alpha) \hat{j}
\end{aligned}$$

During rolling, in each of the canals with subscripts a, r ($a = n, c, \phi$; $r = n, n$) there is induction of pressure [1] P_{ar} :

$$P_{ar} = -2\rho S_{ar} (\cos \theta \cdot \hat{n} \cdot \hat{n}_{ar} + \sin \theta \cdot \hat{n} \cdot \hat{n}_{ar}) \quad (4)$$

where S_{ar} is the area covered by the semicircular canal; ρ is density of endolymph; $\hat{n}_{ar}k$, $\hat{n}_{ar}j$ and $\hat{n}_{ar}i$ are projections of normal $\hat{n}_{ar}(t)$ on unit vectors $\hat{k}$, $\hat{j}$ and $\hat{i}$ at the time we start analyzing processes in the labyrinth.

Movement of endolymph in the canals can be described by a system of equations [1]:

$$\vec{U}_r = M_r \vec{U}_r = M_r \vec{P}_r \quad (5)$$

$\vec{U}_r = \{U_{ar}\}_1^n$ — vector of endolymph displacement in labyrinth canals;

$\vec{P}_r = \left\{ \frac{P_{ar}}{K_{ar}} \right\}_1^n$ — vector of pressure in labyrinth canals;

K_{ar} — coefficient of cupular elasticity

$$M_r = \begin{bmatrix} b'_{11} & b'_{12} & 0 \\ b'_{21} & b'_{22} & 0 \\ 0 & 0 & b'_{33} \end{bmatrix}$$

$$b'_{11} = \frac{K_{ar}}{\Delta r} \left(R_{cr} - R_{nr} \frac{d^2_{cr}}{d^2_{nr}} \right)$$

$$\begin{aligned}
b'_{11} &= -\frac{\eta_{cr}}{\Delta r} R_{cr} \frac{d^2_{cr}}{d^2_{cr}}, \\
b'_{22} &= -\frac{\eta_{cr}}{\Delta r} \left(R_{cr} + R_{cr} \frac{d^2_{cr}}{d^2_{cr}} \right), \\
b'_{31} &= -\frac{\eta_{cr}}{\Delta r} R_{cr} \frac{d^2_{cr}}{d^2_{cr}}, \\
b'_{32} &= \frac{\eta_{cr}}{R_{cr}}; \Delta r = R_{cr} R_{cr} + R_{cr} \cdot R_{cr} \frac{d^2_{cr}}{d^2_{cr}} + \\
&\quad + R_{cr} \cdot R_{cr} \frac{d^2_{cr}}{d^2_{cr}}
\end{aligned}$$

(subscript indicating this parameter is referable to a common limb), $R_{cr} = \frac{32\eta l_{cr}}{d^3_{cr}}$ is the coefficient of resistance of viscous friction in the canal ($l = \Phi, C, H, H$), η is the coefficient of viscosity, l_{cr} is the length of the canal or common limb [crus commune] and d_{cr} is their diameter.

The result of solving the system of linear differential equations (5) with initial values of $\bar{U}_p(0) = \bar{U}_{p0}$ ($p = n, n$) will be vector functions $\bar{U}_p(t)$, determined at interval $t \in [0, T]$.

Hereafter, we shall be concerned only with the special solution of $u_p^s(t)$ of system (5) corresponding to the established oscillations in the canals under the influence of compelling pressure forces.

In order to estimate the absolute angular velocity by means of canal reactions, we inserted ancillary variables:

$$\begin{aligned}
g(t) &= (u_{\Phi n}(t) - u_{cn}(t)) / 2; \\
f(t) &= (u_{cn}(t) - u_{\Phi n}(t)) / 2; \\
q(t) &= (u_{cn}(t) - u_{cn}(t)) / 2.
\end{aligned}$$

These variables are in essence the mean reactions of canals whose planes are parallel. Let us form vector $\bar{v} = v_i \bar{i} + v_j \bar{j} + v_k \bar{k}$ of estimation of absolute angular velocity, the components of which we shall determine as follows:

$$\begin{aligned}
v_i &= \lambda_i (g(t) - f(t)); v_j = \lambda_j (g(t) - f(t)); \\
v_k &= \lambda_k q(t).
\end{aligned}$$

where λ_i , λ_j and λ_k are constant factors chosen from the prerequisite of minimal mean-square error of approximation of components v_i , v_j and v_k to the corresponding

components of γ_i , γ_j and γ_K of the vector of absolute angular velocity in time interval $\Delta T \approx T$.

Description of calculations: The system of equations (5) was solved on a computer by the Euler method with integration spacing of $h = 0.1$ s in time interval $T = 40$ s, with the following values for system parameters: $\mu = 1 \text{ g} \cdot \text{cm}^{-3}$, $l_{AP} = l_{CP} = l_{BP} = l_{HP} = 0.02 \text{ cm}$, $\eta = 0.015 \text{ Pa [poise?]} [3]$, $\vec{u}_{p0} = (0, 0, 0)$, $r = \Pi, \Pi$. When calculating K_{AP} the time constant of the transient process in the canal was considered to be 10 s.

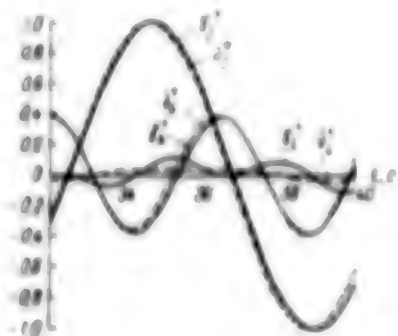


Figure 2.

Relative values of γ_i^0 , γ_j^0 and γ_K^0 (solid lines) of projections of vectors of absolute angular velocity and estimates thereof v_i^0 , v_j^0 and v_K^0 (dash lines) from reactions of semicircular canals

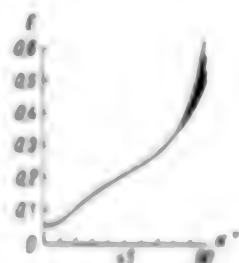


Figure 3.

Mean-square error of approximation of vector of absolute angular velocity of reactions of semicircular canals (calculation for four pairs of human labyrinth preparations)

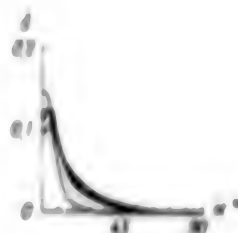


Figure 4.

Relative decline of error of approximation of components of absolute angular velocity to reactions of vertical canals with consideration of influence of crux commune

The geometric characteristics of the semicircular canals l_{AP} , S_{AP} and common limb l_{HP} ($a = \Phi, C, \Pi$; $r = \Pi, \Pi$) were determined for four pairs of human labyrinth preparations made by the corrosion method [4, 5], with consideration of angles of orientation of the labyrinths in the skull [6, 7]. The values of $\vec{u}_{\Pi}^a$, $\vec{u}_{\Pi}^b$ displacements of endolymph corresponding to the established processes in the canals were isolated in interval $\Delta T = 8$ s at the end of the total interval T for solving the system. We selected values typical of a medium sized trawler as the parameters of harmonic functions describing the rolling of a ship [8]:

Figure 2 illustrates approximation of relative values of $\gamma_i^0 = \frac{\gamma_i}{\gamma_m}$, $\gamma_j^0 = \frac{\gamma_j}{\gamma_m}$,

$\gamma_K^0 = \frac{\gamma_K}{\gamma_m}$ of projections γ_i , γ_j and γ_K of the vector of absolute angular velocity

$\bar{v}(t)$ ($v_m = \max(v_L, v_J, v_K)$) $\in [T-\Delta T, T]$) to relative values of $v_L^0 = \frac{v_L}{v_m}$, $v_J^0 = \frac{v_J}{v_m}$, $v_K^0 = \frac{v_K}{v_m}$ of projections v_L , v_J and v_K of vector $\bar{v}(t)$ plotted from the reactions of one of the 4 pairs of labyrinths with $\alpha = 0$.

Figure 3 illustrates the function of overall mean-square error of approximation E of relative values of v_L^0 , v_J^0 and v_K^0 of projections of vector $\bar{v}$ by relative values of v_L^0 , v_J^0 and v_K^0 of projections of vector $\bar{v}$ for all four pairs of labyrinths over time interval ΔT .

Error E increases drastically with high values of $\alpha \in [20, 90^\circ]$. At the same time, there is a certain range of angular deviations of $\alpha \in [0, 10^\circ]$ where the error of approximation does not grow, and this is apparently of substantial biological significance, since it renders the vestibular system insensitive to errors of initial placement of the system for angle α in relation to the normal position of $\alpha = 0$.

It is interesting to determine the role of the crus commune of vertical canals in the process of approximation by the vector of absolute angular velocity of the canal reactions. Since its role affects only the reactions of vertical canals [1], we calculated separately for v_L^0 and v_K^0 , in time interval ΔT , the overall mean-square errors of approximation E_n in the presence of the common limb and E_0 in its absence. Figure 4 illustrates the relative value of:

$$\delta = \frac{E_n - E_0}{E_0}$$

which is the change in error of approximation induced by the influence of the common limb as a function of magnitude of angle α for the 4 pairs of labyrinth preparations. On the basis of Figure 4, it can be concluded that there is slight improvement of quality of approximation ($\sim 10\%$) in the presence of the common limb and natural head position in relation to the body ($\alpha = 0$).

Thus, the results of our studies of hydromechanical reactions of the semicircular canals in the presence of periodic exogenous influences of the ship-rolling type, which were conducted using mathematical modeling on a computer, revealed that these reactions can serve as rather accurate approximation of the vector of absolute angular velocity of the human body. With the head in normal position in relation to the body, the influence of crus commune is manifested by improved approximation of components of absolute angular velocity that are represented by the vertical canals.

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HUMAN COLOR DISCRIMINATION DURING VESTIBULAR STIMULATION AFTER EXPOSURE TO BRIGHT LIGHT

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981 pp 66-70

[Article by Zh. M. Kudryashova and A. A. Shipov, submitted 28 Feb 80]

[English abstract from source] Manned studies have demonstrated that eye exposure to light of 2.5×10^3 – 50.0×10^3 nit leads to transient color blindness, decrease in the central color, bright contrast sensitivity and decline in functional stability of color discrimination. Pre-exposure to light luminosity of 50.0×10^3 nit enhances the decrease in functional stability of color discrimination due to vestibular stimulation. This is accompanied by a decline in vestibular tolerance. Mechanisms of the changes in color discrimination and resistance to vestibular stimulation are discussed.

[Text] The ability to discriminate colors is an important function of the human eye. It is of particular importance for operators of moving transportation systems to have correct color discrimination, since presence in such systems involves exposure to unusual vestibular stimuli. Operator work in such systems is often associated with drastic changes in color modes. Thus, on clear sunny days, pilots and drivers of surface vehicles generally work at levels of $2 \cdot 10^3$ to $35 \cdot 10^3$ nit background light. Brightness can fluctuate from 20 to $50 \cdot 10^3$ nit in the cabins of spacecraft.

In this work, we tested man's color discriminating function in a situation that is often encountered when driving different types of vehicles, namely, during vestibular stimulation after exposure to very bright light.

Methods

We conducted this study on 13 healthy subjects of both sexes ranging in age from 20 to 35 years, with normal color discrimination.

The studies were conducted in a room with average spherical illumination of 30-40 lux in the photopic range.

The subject was seated in a chair in front of a binocularly visible white reflecting ($K = 0.96$) screen 20×20 cm², at an angle of 15-17°, situated 60 cm from the

eyes. The background brightness of the screen and of the test tables constituted 60 lux on white (20 nit). Photometric brightness of the screen was measured with a Yu-16 lux meter.

For light lasting 10 s, we used luminances of $2.5 \cdot 10^3$, $4.0 \cdot 10^3$, $7.0 \cdot 10^3$, $12.5 \cdot 10^3$, $25.0 \cdot 10^3$ and $50.0 \cdot 10^3$ nit.

Immediately after exposure to the light, the chair was rotated. Vestibular stimuli were simulated by the system of I. I. Bryanov [1]. In all, there were 15 rounds of rotation. Rotation was stopped if grade II vestibulovegetative reactions (VVR-2) occurred during rotation.

For objective recording of autonomic reactions before and immediately after rotation we determined the heart rate (HR) from the R-R interval; arterial pressure (AP) according to N. S. Korotkov, central retinal artery pressure (CRP), caliber of central veins (CCV) and arteries (CCA) of the retina.

Before exposure to light (background level of 20 nit), immediately after it and after termination of rotation, we determined the time of loss of color discrimination, thresholds of color and brightness contrast sensitivity, time thresholds of adisparopia (ADP). We also measured ADP thresholds during the intervals between rotations through the 8th round, after the 10th and 15th rounds, and in the 5th, 10th and 15th min of the aftereffect period. The method we used is described in greater detail in [2].

Control (without light exposure) rotations were made after 10 min of light adaptation to the photopic level of illumination (20 nit). The subjects who did not develop clinically demonstrable autonomic reactions after 15 rounds formed the group with vestibular stability. Individuals who developed VVR-2 during control rotations constituted the group with vestibular instability.

These studies also enabled us to assess the effect of brief exposure to bright light on vestibulovegetative stability of man.

The obtained data were submitted to statistical processing with the use of the criterion of Student ($P < 0.05$).

Results and Discussion

In the background period, the subjects immediately distinguished the color of the presented object. The thresholds of color and contrast brightness sensitivity were not the same for different parts of the visible spectrum: they were highest for the short-wave part and lowest for the part with average waves (Figure 1, a and b). With increase in intensity of light, the time of loss of color discrimination increased and constituted 20.6 ± 1.1 s for red, 19.5 ± 1.3 s for green and 60.9 ± 1.8 s for blue after exposure to light of maximum brightness ($50 \cdot 10^3$ nit). There was also elevation of thresholds of color and contrast brightness sensitivity (see Figure 1a). There were different changes in ADP time thresholds with increase in intensity of light. In the range of luminance of up to $4 \cdot 10^3$ nit, the ADP thresholds dropped drastically (to less than one-half), then the rate of decline diminished appreciably ($4 \cdot 10^3$ – $12 \cdot 10^3$ nit range), while with further increase in brightness it increased again (see Figure 1b).

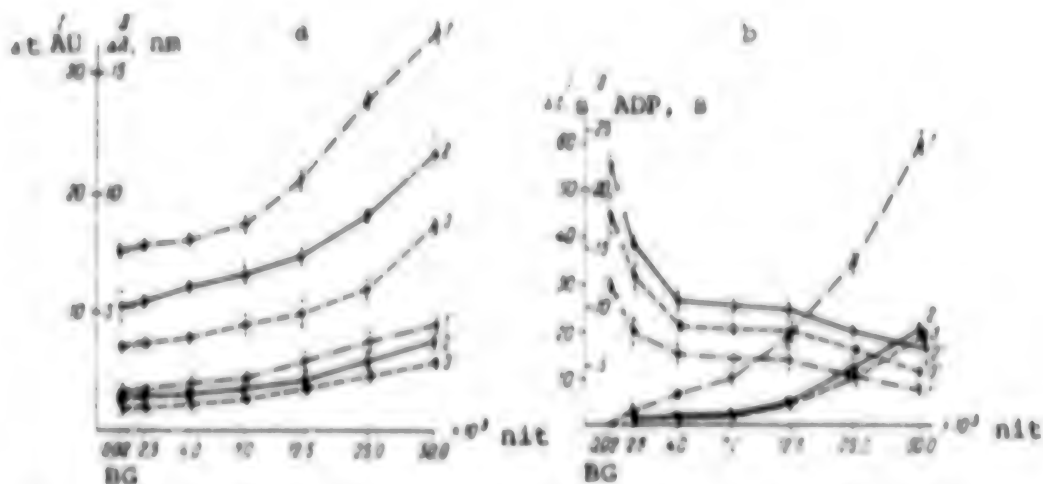


Figure 1. Parameters of color discrimination as a function of brightness of illumination. X-axis, brightness on a logarithmic scale

- a) thresholds of brightness (axis I, curves 1, 2, 3) and color (axis II, curves 1', 2', 3') contrast sensitivity
 b) time of loss of color discrimination (axis I, curves 1, 2, 3) and ADP time thresholds (axis II, curves 1', 2', 3')
- 1, 1') for blue 2, 2') for red 3, 3') for green
- AU) arbitrary units BG) background

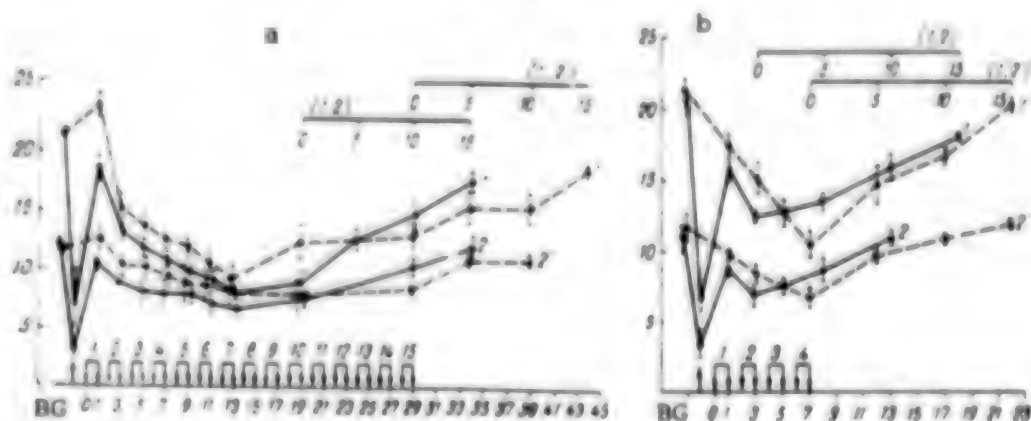


Figure 2. Changes in ADP time thresholds in group with vestibular stability (a) and vestibular instability (b). X-axis, current time (min); digits over arrows designate sequential numbers of rotation rounds. The isolated arrow shows time of illumination. The horizontal scales on the top refer to time of aftereffect of vestibular stimuli (min) [BG--background].

- 1, 2) for red and blue, respectively, during vestibular stimulation without exposure to light
 1', 2') the same with prior exposure to light of $50 \cdot 30^3$ nit.

Thus, all of the tested characteristics of color discrimination changed with brief exposure of the eyes to very bright light.

Parameters of peripheral and retinal circulation after vestibular stimulation with prior exposure to light of $50 \cdot 10^3$ nit (M:m)

Group	Conditions	CRP, mm Hg	CCV, μ m	CCA, μ m	HR/min	AP _{min}	AP _{max}
All subjects	Background	38.8 ± 1.8	160.7 ± 1.9	81.8 ± 2.2	78.5 ± 2.0	71.5 ± 1.9	116.4 ± 3.8
With vestibular stability	Not exposed	42.0 ± 0.8	170.0 ± 2.4	80.0 ± 1.8	76.9 ± 0.7	78.0 ± 1.7	105.0 ± 1.9
	Exposed to light	45 ± 1.6	178.0 ± 1.9	85.0 ± 2.4	78.0 ± 1.0	65.0 ± 1.9	115.0 ± 1.6
With vestibular instability	Not exposed	39.0 ± 2.7	170.0 ± 2.5	82.0 ± 1.5	74.0 ± 0.9	80.0 ± 0.9	128.0 ± 0.8
	Exposed to light	47.0 ± 0.6	180.0 ± 2.1	91.0 ± 2.1	69.0 ± 1.2	94.0 ± 1.2	123.0 ± 1.1

No reliable changes in parameters of either retinal or peripheral circulation were demonstrated in the range of $20-25 \cdot 10^3$ nit. It is only with brightness of $50 \cdot 10^3$ nit that the changes were reliable. Thus, there was elevation of AP and CRP (by 8 mm Hg), HR and CCV.

As was demonstrated previously [2], only the time thresholds of ADP decline with vestibular stimuli without exposure of the eyes to light (control studies), unlike the effect of bright light; the thresholds of color and brightness contrast sensitivity remain unchanged. During control rotation, it was found that 5 out of 13 subjects had vestibular stability and 8 had vestibular instability.

We also failed to demonstrate reliable changes in thresholds of color and brightness sensitivity as a result of vestibular stimulation after exposure to light. With exposure to brightness of $20-25 \cdot 10^3$ nit there were no changes either in ADP time thresholds, as compared to the results of control tests. At brightness level of $50 \cdot 10^3$ nit, the increase in ADP threshold after the first round of rotation was reliably less marked than in the control studies, in the group with vestibular stability, as well as with vestibular instability (Figure 2, a and b). Upon subsequent rotation (up to the 10th round for the group with vestibular stability and 2d round for the one with instability) the thresholds were also lower (although unreliably) than during vestibular stimulation without prior exposure to light.

The subjects discriminated colors immediately after rotation, both in the control tests and with the use of vestibular stimuli after exposure to light.

The changes in parameters of retinal and peripheral circulation during vestibular stimulation following exposure to light with brightness of background ranging from $2.5 \cdot 10^3$ to $25.0 \cdot 10^3$ nit did not differ reliably from the results of the

control studies [2]. However, with maximum luminance ($50 \cdot 10^3$ nit), the observed changes were more profound in both groups (see Table).

Preliminary exposure to light with background brightness of $2.5 \cdot 10^3$ to $12.5 \cdot 10^3$ nit did not alter resistance to vestibular stimuli. At the same time, after exposure to luminance of $25 \cdot 10^3$, VVR-2 developed in 3 out of 5 in the group with vestibular stability after 10 rounds of rotation, while 5 out of 8 subjects in the group with vestibular instability tolerated only 1-2 rounds of rotation, whereas in the control studies they withstood 4 rounds. With background brightness of $50 \cdot 10^3$ nit, we observed further decline of vestibulovegetative resistance of the subjects. Thus all 5 vestibulo- [middle of sentence missing from source] ... presented VVR-2, and all 8 in the group with vestibular instability endured only 1-2 rounds of rotation.

Thus, our studies revealed that drastic changes in illumination, created by creating light of $2.5 \cdot 10^3$ - $50 \cdot 10^3$ nit, lead to temporary color blindness, diminish central color and brightness contrast sensitivity, as well as lower the level of functional stability of color discrimination (ADP time thresholds). A deterioration of color discrimination was demonstrated over the entire tested spectrum of wavelengths, but it was less marked in the medium-wave range, which is consistent with conceptions of the special functional role of medium-wave radiation [3]. It can be assumed that the decline of color and brightness contrast sensitivity with bright illumination occurs mainly due to processes of readaptation on the receptor and first nerve levels of the retina [4]. The decline of level of stability of color discrimination probably occurs not only due to purely retinal processes, including receptor ones, but chiefly due to development of inhibitory processes in the higher optic centers [2].

The greater decline of functional stability of color discrimination, which was observed with delivery of vestibular stimuli [2], after exposure to light with brightness of $50 \cdot 10^3$ nit is indicative of the fact that the residual effects of exposure to luminance close to the solar constant persist for a rather long time.

We must call attention to the fact we established, that in the case of fluctuation of brightness from $2.5 \cdot 10^3$ to $12.5 \cdot 10^3$ nit, which is usually encountered by man in ground vehicles, there are no changes in resistance to vestibular stimuli. Exposure to light of $25 \cdot 10^3$ nit or more diminishes vestibular stability. It may be assumed that blinding light of this intensity depresses the function of the cerebral cortex. Cortical inhibition of autonomic centers diminishes [5], and the vestibulovegetative reactions become particularly marked.

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EFFECT OF SPECIFIC VOLUME ON FORMATION OF ATMOSPHERE IN SEALED COMPARTMENTS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
pp 70-72

[Article by V. P. Savina, Yu. G. Nefedov, T. I. Kuznetsova, V. Ye. Ryzhkova,
K. N. Mikos and K. V. Grishina, submitted 5 Jul 79]

[English abstract from source] Atmosphere pollution with noxious gaseous trace contaminants exhaled by man in an enclosure was investigated as a function of free volume per man. The parameter was shown to depend on the environmental conditions: with increase in free volume the total level of atmosphere pollution decreased, being proportional to the concentration of gaseous trace contaminants in the exhaled air. Experimental curves of accumulation of gaseous chemicals exhaled by man were built.

[Text] In view of the development of space technology, which enables man to remain in orbit or participate in a distant space flight for a long period of time, it is quite important to determine the optimum volume per crew member. This problem is being solved in several directions. Questions of psychophysiology, temperature and humidity conditions and pollution of the air environment by toxic gas impurities are quite important. We have examined this problem from the standpoint of formation of the habitat environment according to composition of deleterious impurities, the source of which is man himself.

It was previously established that man discharges up to 400 chemical compounds as a result of his vital functions. Perspiration, exhaled air and intestinal gases are the main sources of atmospheric pollution when man is isolated in a sealed compartment for a long period of time. Studies involving isolation of man in a pressurized compartment for different periods of time identified the main chemicals and determined their quantitative composition [1, 2]. As shown by the experience of submarine medicine, a limited volume often leads to adverse phenomena [3, 4].

Generalization and analysis of data in the literature made it possible to determine the absolute free volume necessary to man during a long stay in compartments of the pressurized [sealed] type. They were found to constitute 6, 8, 12 and 24 m³/per person. The following volume variants exist: minimum acceptable, acceptable and somewhat above the optimal.

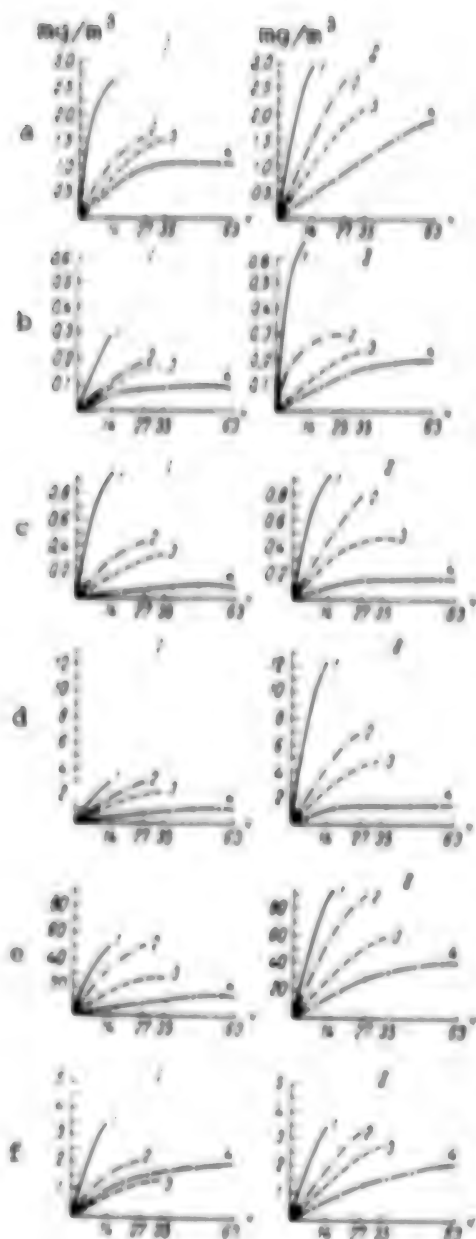


Figure 1.

Changes in concentration of acetone (a), acetaldehyde (b), methanol (c), ethanol (d), methane (e) and diethyl ether (f) in 6, 8, 12 and 24 m³/person pressure chambers (1-4 respectively), in normal (I) and experimental (II) conditions

Results and Discussion

On the basis of the experimental data, we plotted the curves of accumulation of toxic impurities in the pressure chamber. Figure 1 illustrates the curves of such accumulation in different-sized chambers at the early stage of accumulation

Methods

The distinctions of formation of the habitat as a function of free volume per person were studied in 16 tests lasting 7-8 days each, with the participation of 36 essentially healthy male volunteers.

The studies were conducted at a comfortable temperature and relative humidity (temperature 16±1 and 21±2°C, relative humidity 30-70% in 4 tests), as well as under more difficult conditions (33±1 and 35±1°C, relative humidity 90% in 4 studies).

In order to examine the rate of accumulation of deleterious impurities discharged by man, the initial period of each test did not involve the use of methods for purifying the atmosphere and was simulated by the time that a concentration of 4-5% carbon dioxide was reached which, in the opinion of specialists, has no toxic effect on man.

We examined the air environment, condensates of atmospheric moisture and air exhaled by the subjects to determine the levels of acetone, acetaldehyde, methanol, ethanol, methane, diethyl ether, carbon monoxide, ammonia and amino compounds, and fatty acids from general oxidation. We used gas chromatography, colorimetry, nephelometry and linear colorimetric methods. A Tsvet 126 chromatograph was used for gas chromatographic analysis. Chromatography conditions: flame ionization detector, column 1.5 m in length filled with porapak Q [?], column temperature 150°C, detector temperature 135°C, velocity of gas carrier helium and nitrogen 40 ml/min. We used 1-ml samples for each analysis.

thereof with the system of purifying the atmosphere turned off. These periods lasted an average of 14, 27, 35 and 63 h for chambers with 6, 8, 12 and 24 m³/person, respectively. The curves indicate that there was an increase in concentration of acetone, acetaldehyde, methanol, ethanol, methane and diethyl ether in the air environment of the pressurized chambers. The most intensive accumulation of toxic microimpurities was noted in the smaller chambers.

There was faster accumulation of toxic impurities emitted by man under more difficult conditions (raising temperature to 32-36°C and relative humidity to 90%). Thus, when the men were submitted to the more difficult microclimate, as compared to optimum temperature and humidity in the pressure chamber, there was an increase by more than 70% in acetone concentration over the same period of time and 130% increase in acetaldehyde.

Figure 2 illustrates the experimental curves of mean rate of accumulation of organic microimpurities as a function of free volume. This is an exponential function.

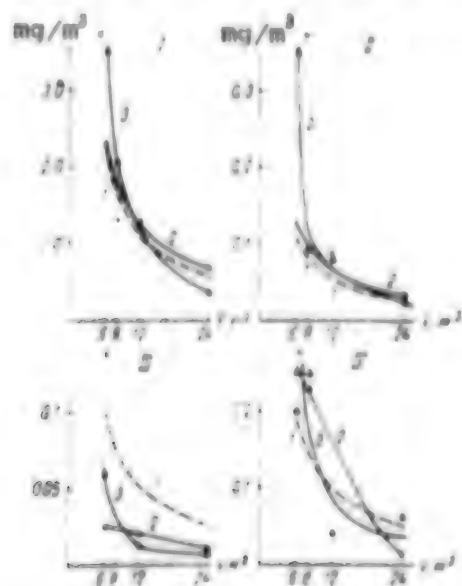


Figure 2.

Rate of accumulation of methane (I), acetone (II), methanol (III) and ethanol (IV) in pressure chamber air as a function of free volume per person

- 1) estimated data
- 2) normal conditions
- 3) experimental [difficult] conditions

we compared concentrations of ammonia, acetone and aldehydes in the condensate of atmospheric moisture.

In addition, we found that, with established equilibrium between discharge of toxic impurities by man and absorption thereof by the atmosphere-purification system, the level of pollution of the air environment by toxic impurities is inversely proportional to the specific volume per person.

With increase in free volume there is an appreciable decline in rate of accumulation of toxic impurities in the atmosphere of the chamber. In the same figure, the dash line illustrates the estimated mean rates of discharge of various chemicals when man inhales air in a pressurized chamber with standard microclimate, diet, exercise, work and rest schedule. We were impressed by the fact that the difference between rates of accumulation of toxic impurities in the air of the chamber under normal and experimental conditions is at a maximum when there is up to 6 m³/person. With increase in volume this parameter declines and reaches a minimum value for almost all of the assayed components with volumes of 12 and 24 m³/person.

The results of examination of the composition of toxic impurities in a condensate of atmospheric moisture revealed that oxidizability of the condensate was considerably greater with 6 and 8 m³/person; with 12 and 24 m³/person, the condensate was considerably purer. An analogous pattern was demonstrable when

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EFFECT OF SPACE FLIGHT FACTORS ON ULTRASTRUCTURE OF SKELETAL MUSCLES

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
pp 72-77

[Article by K. D. Rokhlenko and Z. F. Savik, submitted 2 Aug 79]

[English abstract from source] By electron microscopy ultra-structures of myofibers of the soleus and gastrocnemius muscles of rats flown in zero-g and 1 g were examined. It was found that 4,5-9 hours postflight the soleus of weightless rats showed focal destruction of the contractile and mitochondrial systems accompanied by metabolic changes in muscle fibers. Exposure to artificial gravity partially prevented changes in muscle fibers. Examinations of muscle fibers 25 days postflight demonstrated that the changes were reversible. No changes were seen in the mixed--gastrocnemius--muscle of both animal groups.

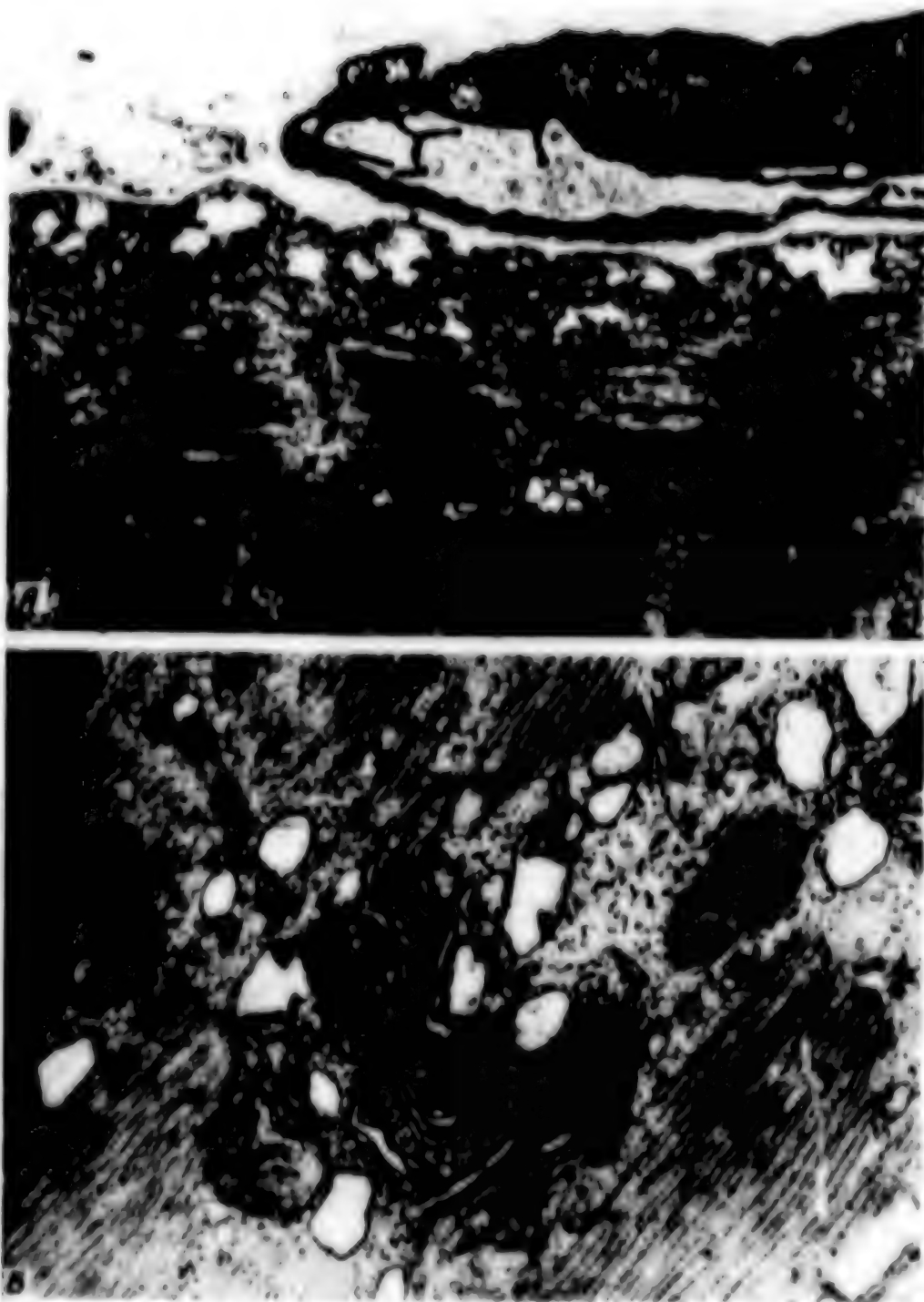
[Text] Studies conducted aboard the Cosmos-605 and Cosmos-782 biosatellites revealed that atrophic and dystrophic changes develop in muscle fibers, under the influence of space flight factors, and they are associated with impairment of their metabolism [1-4]. We submit here the results of electron microscopic studies of rat skeletal muscles after a flight aboard the Cosmos-936 biosatellite.

Methods

We used electron microscopy to study red (soleus) and mixed (gastrocnemius) muscles of rats flown aboard Cosmos-936 for 18.5 days and sacrificed 4.5-9 h and 25 days after the flight. The objectives and conditions of the experiments were described in detail in [5]. In all, we used 45 rats in the experiment. Nine of the 20 animals aboard the satellite were exposed to artificial gravity throughout the flight. Fifteen animals from the ground-based synchronous experiment (which simulated all of the space flight factors, with the exception of weightlessness) and 10 rats maintained in the vivarium served as a control.

Samples of muscles were fixed in 2.5% glutaric aldehyde solution for 3 days, and additionally treated with OsO₄, according to Millonig [6], then imbedded in araldite.

Sections were cut on an LKB ultratome, contrasted with lead citrate according to Reynolds [7] and viewed under a UEMV-100L electron microscope.



Ultrastructure of fibers of rat soleus after flight in weightlessness
aboard Cosmos-936

- A) 4.5-9 h after flight; magnification 25,000 $\times$; increased distance between myofibrils; dilated tubules in cisterns of sarcoplasmic reticulum; mitochondrial swelling
- B) 4.5-9 h after flight; 40,000 $\times$; formation of myelinoid structures in muscle fiber sarcoplasm

Key to figure (continued) [continuation of figure on p 109]

B) 4.5-9 h after flight; 25,000 $\times$; drastic increase in amount of glycogen granules between myofibrils

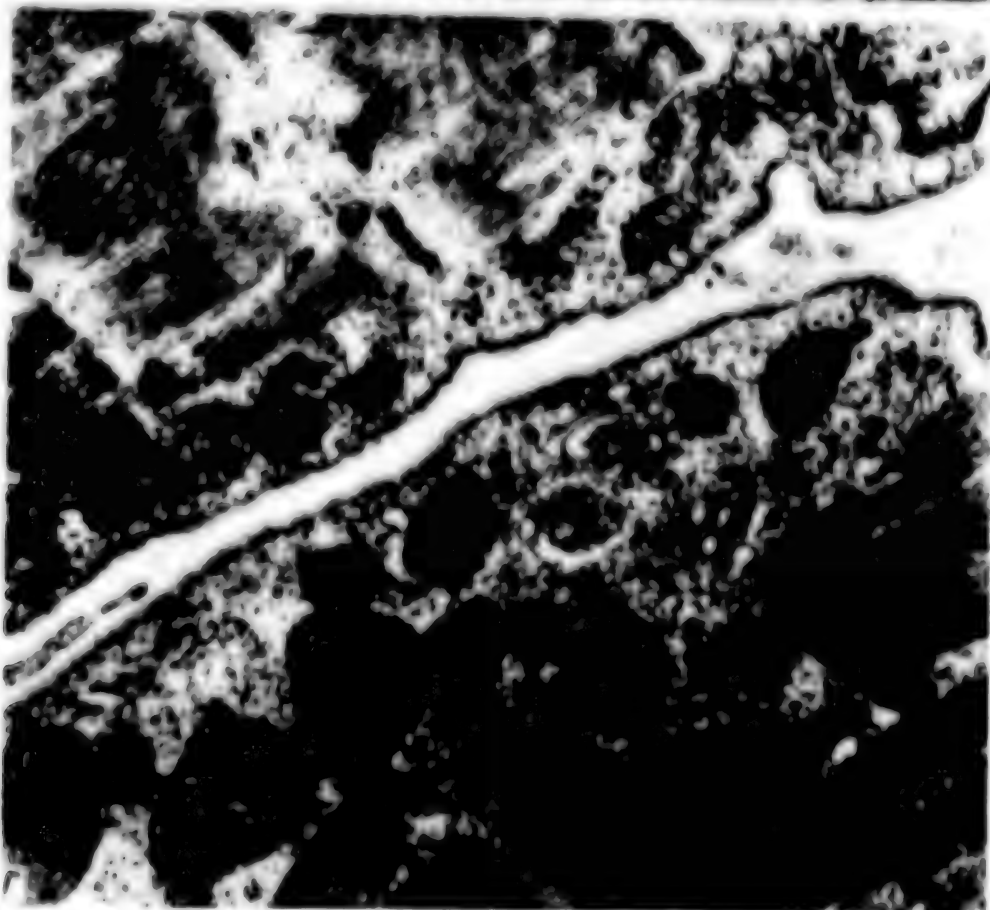
F) 25 days after flight; 18,000 $\times$; subsarcolemmar zone of muscle fiber; granular sarcoplasmic reticulum; numerous polyribosomes

Results and Discussion

Histological examination of semithin tissue sections from animals of all groups failed to demonstrate appreciable structural changes in the soleus and gastrocnemius, not counting a few foci encountered in some parts of the soleus muscle of rats exposed to weightlessness and those in the ground-based asynchronous experiment. In these regions, we observed loss of striation and widening of spaces between muscle fibers. Electron microscopy revealed destructive changes in both contractile and mitochondrial elements in such parts of the soleus of rats that had been submitted to weightlessness and were sacrificed 4.5-9 h after the flight. The changes in contractile elements consisted of increase in distance between myofibrils and presence of local foci of separation of myofibrils (see Figure, A). Occasionally, the Z band in such fibers presented a zigzagged course. Isolated fibers presented displacement of homologous disks and bands. The greatest changes were referable to the mitochondria: the matrix of many of them was clear, with appreciable decrease in number of cristae; some mitochondria were markedly vacuolized, with partially or completely destroyed cristae; quite often, there were myelinoid elements next to the mitochondria or within them (see Figure, B). The sarcoplasmic reticulum was fragmented, and not infrequently the terminal cisterns were dilated. Such changes in the contractile and mitochondrial systems were focal in nature and severity thereof varied in different animals.

A typical finding in the soleus of animals submitted to weightlessness was deposition of excessive amounts of glycogen (see Figure, B) and drops of lipids. The interfibrillar spaces, as well as subsarcolemmar and perinuclear zones were "stuffed" with glycogen granules. They were so tightly packed that the cisterns of the sarcoplasmic reticulum in areas of accumulation of glycogen were deformed. Incorporation of lipids was represented by round drops with homogeneous or typical wavy structure. As a rule, the droplets of lipids were in close contact with the mitochondrial membrane. Their size varied widely, sometimes reaching a considerable value, 1.5-2 μm (versus the normal of 0.3-1.0 μm).

We also encountered in the soleus some dying, as well as atrophied, muscle fibers; the interstitial spaces between such fibers were widened and contained more than the normal amount of connective tissue cells, mature fibrous structures and, occasionally, remnants of disintegrated muscle fibers. There was an increase in number of nonfunctional capillaries. As a rule two out of 4-6 capillaries supplying blood to one muscle fiber had a collapsed wall; however, the ultrastructure of endothelium forming their wall did not differ from normal.



There were focal changes in the soleus, but they were less marked and less extensive in animals submitted to artificial gravity 4.5-9 h after landing, as well as in animals sacrificed at the same time that had been submitted to weightlessness during the flight. We did not observe atrophy of muscle fibers, myelinoid elements were seldom encountered, and there was insignificant mitochondrial swelling. Unlike the figures for animals submitted to weightlessness, glycogen and lipid levels in the soleus of rats submitted to artificial gravity were the same as in the rats in the vivarium control group. The blood capillaries were dilated and filled with erythrocytes; the ultrastructure of their walls did not differ from normal.

The changes were less marked and involved only isolated sarcomeres in animals from the ground-based synchronous experiment.

A comparison of ultrastructural changes in the soleus warrants the statement that there is the same type of change in all experimental groups of rats. It must be noted that initial qualitative changes in the soleus were observed with experimental simulation of weightlessness by means of restricting animal movement [8].

Thus, we observed focal destructive and dystrophic, as well as distinct metabolic, changes in the soleus of rats exposed to weightlessness; evidently they are related to the lack of a functional load on the skeletomuscular system. The destructive changes demonstrated in soleus muscle fibers 4.5-9 h after the flight were reversible, and they were not demonstrable 25 days after the biosatellite landed.

Unlike animals examined immediately after landing, 25 days after the flight we encountered many myosatellitecytes with well-developed granular sarcoplasmic reticulum, lamellar complex and a large number of polyribosomes, which was indicative of activation of synthetic processes in these cells. We were impressed by the widening of perinuclear and subsarcolemmal zones of muscle fibers, in which there were mitochondria, lysosomes, microcorpuscles, vacuoles and cisterns of the lamellar complex, and cytogranules (see Figure, Γ), which was also indicative of intensification of protein synthesis.

The blood capillaries were dilated, plethoric, and the cytoplasm of endothelial cells contained a significant number of pinocytotic vesicles. In some regions, the layer of perivascular connective tissue and connective tissue situated between muscle fibers were enlarged and represented by mature collagen fibers and cellular elements with signs of high functional activity.

Thus, 25 days after the flight, the soleus muscle fibers presented activation of intracellular regeneration, which is apparently related to the drastic increase of the load on this muscle with the transition from weightlessness to earth's gravity.

We failed to observe any ultrastructural disturbances in the mixed gastrocnemius, either 4.5-9 h or 25 days after the flight. We were impressed by the presence of many glycogen granules, as in the soleus. The less marked structural changes in gastrocnemius fibers, as compared to those of the soleus, are most probably related to the functional distinctions of this muscle, its metabolism and blood supply [9-11].

Thus, the results of these studies indicate that creation of artificial gravity aboard the Cosmos-936 biosatellite prevented in part development of structural and metabolic changes inherent in weightlessness in the soleus muscle.

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ULTRASTRUCTURE OF THE MYOCARDIUM OF RATS FLOWN ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
pp 77-82

[Article by K. D. Rokhlenko and P. Ya. Mul'diyarov, submitted 20 Jul 79]

[English abstract from source] Hearts of rats flown for 19.5 days aboard the biosatellite Cosmos-936 and decapitated 4.5-9 hours or 25 days postflight were examined electron microscopically. Hearts of weightless rats sacrificed at R + 0 showed marked and consistent changes in capillaries and venules; myelin transformation of membranes of mitochondria and sarcoplasmatic reticulum was seen in cardiomyocytes which did not show lysis. It is assumed that development of myelin bodies and increase in the number of autophagosomes in weightless rats were caused by disintegration of mitochondrial and sarcoplasmatic reticulum structures. Rats exposed inflight to artificial gravity displayed less pronounced submicroscopic changes.

[Text] Deconditioning of the heart has been observed in cosmonauts participating in long term flights [1-4], and this makes it necessary to study the structure, function and metabolism of the myocardium. Studies with the use of electron microscopy must be an integral element of such research, since it permits detection of fine structural changes that are not visible under a light microscope.

Methods

We submit here the results of electron microscopy of the left ventricular myocardium of rats flown aboard Cosmos-936 for 18.5 days. Ten out of 20 rats were exposed to artificial gravity (AG) for the entire flight. The animals were decapitated 4.5-9 and 25 days after landing. In addition, we used 15 animals in a ground-based synchronous experiment, where all space factors were simulated, with the exception of weightlessness. Ten animals were kept in the vivarium and made up the control group. In all, we studied 45 rats.

The presence of rats submitted to AG aboard the biosatellite made it possible to distinguish the effects of weightlessness.

After decapitation of the animals, we rapidly opened the chest, separated the heart and excised a layer of myocardium from the region of the apex of the left

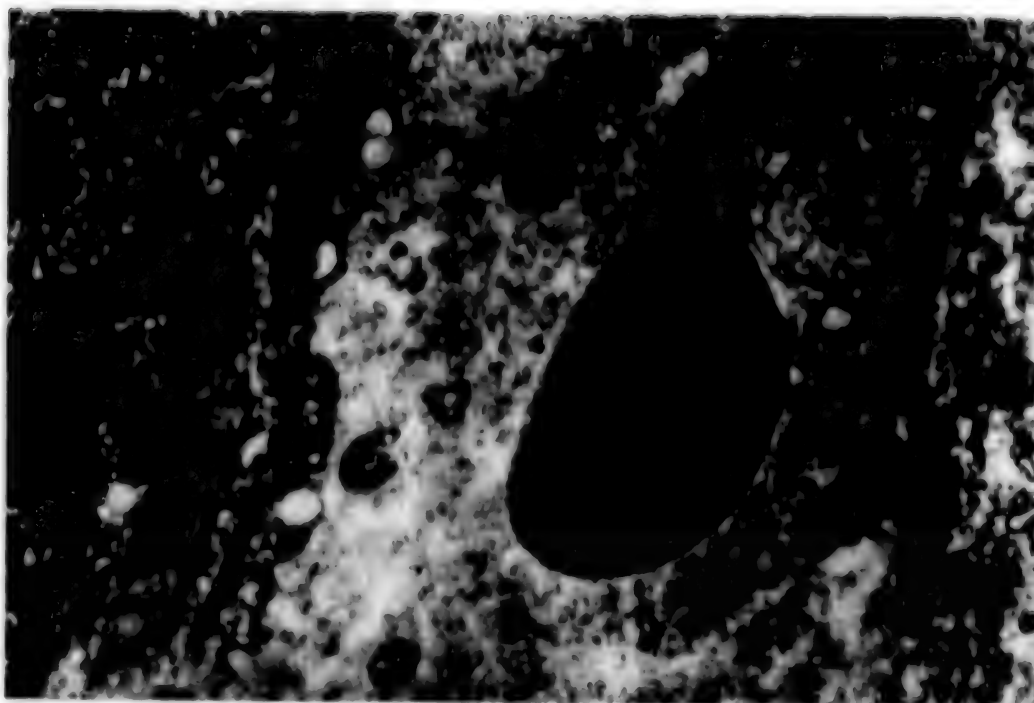


Figure 1. Plasmoorrhagic area containing plasma, erythrocytes and free mitochondria in the myocardium of rats decapitated 4.5-9 h after flight in weightlessness; magnification 12,000×

ventricle, and immediately submerged it into cold 2.5% solution of glutaric aldehyde prepared with 0.1 M phosphate buffer, pH 7.4. Fixation continued for 3 days at room temperature. The myocardial plate was then cut into pieces about 0.5 mm in size, washed in buffered 0.33 M saccharose solution, additionally fixed in 1% OsO₄ according to Millonig, washed, dehydrated in ascending concentrations of alcohol and imbedded in araldite. Sections 0.5-2 μ m thick were stained with 1% toluidine blue and examined under a light microscope. Interesting segments were prepared for electron microscopy.

Ultrafine sections were contrasted with lead citrate and viewed under a UEMV-100L or UYeM-100V electron microscope.

Results and Discussion

Electron microscopy of the left ventricular myocardium of rats exposed to weightlessness during flight and decapitated 4.5-9 h after the satellite landed revealed that the most consistent changes were in the blood capillaries and venules. They consisted of edema of endotheliocyte cytoplasm, appearance of different sized



Figure 2. Segment of myocardium:

- a) clearing of sarcoplasm and nucleoplasm, separation of organelles, mitochondrial swelling in cardiomyocytes of rats decapitated 4.5-9 h after flight under weightless conditions; magnification 10,000×
- b) no changes in myocardium of rats sacrificed 4.5-9 h after flight with exposure to artificial gravity; magnification 7000×

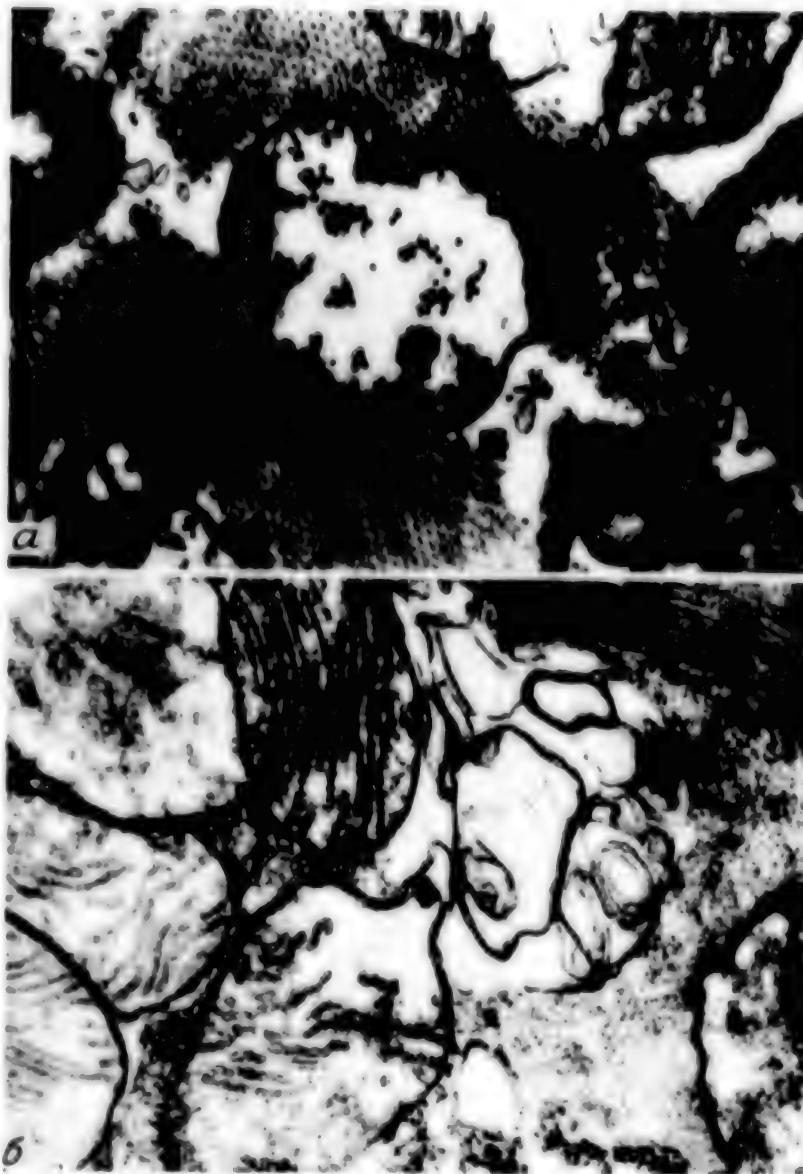


Figure 3. Segment of myocardium (weightlessness, 4.5-9 h after flight)

- a) appearance of glycogen granules in mitochondria of rat cardiomyocytes; magnification 36,000×
- b) myelin transformation of mitochondrial membranes and tubules of sarcoplasmic reticulum 4.5-9 h after flight; magnification 36,000×

vacuoles and myelin bodies in it, swelling of mitochondria and cisternae of the granular endoplasmic reticulum. We often encountered breaks in the endothelium, with lacunae containing plasma, erythrocytes, myelinoid elements and vacuoles between the muscle fibers (Figure 1).

In the cardiomyocytes, the changes were referable mainly to the sarcoplasm and mitochondria. The sarcoplasm of many myocytes was clear, with some degree or other of separation of organelles. There was an increase in number of lipid drops and in their size, while the number of glycogen granules decreased. Most mitochondria appeared swollen, their cristae were fragmented or even destroyed. In the nuclei, there was clearing of nucleoplasm and condensation of chromatin along the nuclear membrane (Figure 2a). It must be noted that these changes were the most marked in rats sacrificed 4.5 h after landing: significant destruction of cristae and vacuolization of mitochondria, breaks in their membranes and glycogen granules in the cleared matrix (Figure 3a). Appearance of glycogen granules in the mitochondria could be attributed to either the fact that the mitochondrial membrane becomes permeable to the enzymes of glycogen synthesis, or presence of breaks in the membrane through which the glycogen granules penetrate. There were areas of microhemorrhages in the myocardium, and isolated mitochondria were observed among the formed blood elements. These changes were less marked in animals sacrificed 6-8 h after landing.

The cardiomyocytes of rats submitted to weightlessness were characterized by myelinoid transformation of mitochondrial membranes and tubules of the sarcoplasmic reticulum. Myelin bodies were demonstrable both within the mitochondria and in their immediate vicinity (Figure 3b). We did not observe appreciable changes in myofibrils, T system of the sarcoplasmic reticulum or lamellar complex. Neither light microscopy (semifine sections) nor electron microscopy revealed atrophy of cardiomyocytes or increase in mass of interstitial connective tissue. Macrophages with many lysosomes and vacuoles with heterogeneous contents were encountered in the areas of microhemorrhages.

The above-described ultrastructural changes were not demonstrable 25 days after the flight, and the electron microscopic findings on the myocardium were almost identical to those made in rats of the vivarium control, with the exception of some increase in number of autophagosomes, in the heterogeneous contents of which we could discern residues of myelinoid structures, some cristae and even whole mitochondria (Figure 4).

The pathological changes in the myocardium were less marked and microhemorrhages were encountered less often in rats exposed to AG 4-9 h after landing, than in rats exposed to weightlessness. In these rats, edema of the endotheliocytes and cardiomyocytes was insignificant; mitochondrial swelling and myelinization of membrane structures of myocyte were either absent or negligible (see Figure 2b). There were no changes in the interstitial layers of the myocardium. On the whole, the electron microscopic findings referable to the myocardium of rats submitted to AG during the flight resembled those on animals in the ground-based synchronous experiment.

To sum up our data, it can be concluded that the ultrastructural changes observed in the myocardium are very similar to those encountered in the presence of diverse forms of tissular hypoxia of the heart. Appearance of such changes in animals submitted to weightlessness can apparently be attributed to the fact that, when the animal changes from a weightlessness state to earth's gravity, the heart

experiences a drastic increase in load, as compared to weightlessness. There may be an inconsistency between the increased load on the heart and its blood supply, which could lead to tissular hypoxia--mitochondrial swelling against the background of edema of the sarcoplasm, damage to mitochondrial membranes and decrease in number of glycogen granules. Tissular hypoxia may become more marked due to damage to the microcirculatory system. This is indicated by the parallel between degree of impairment of microcirculation and severity of cardiomyocyte changes.

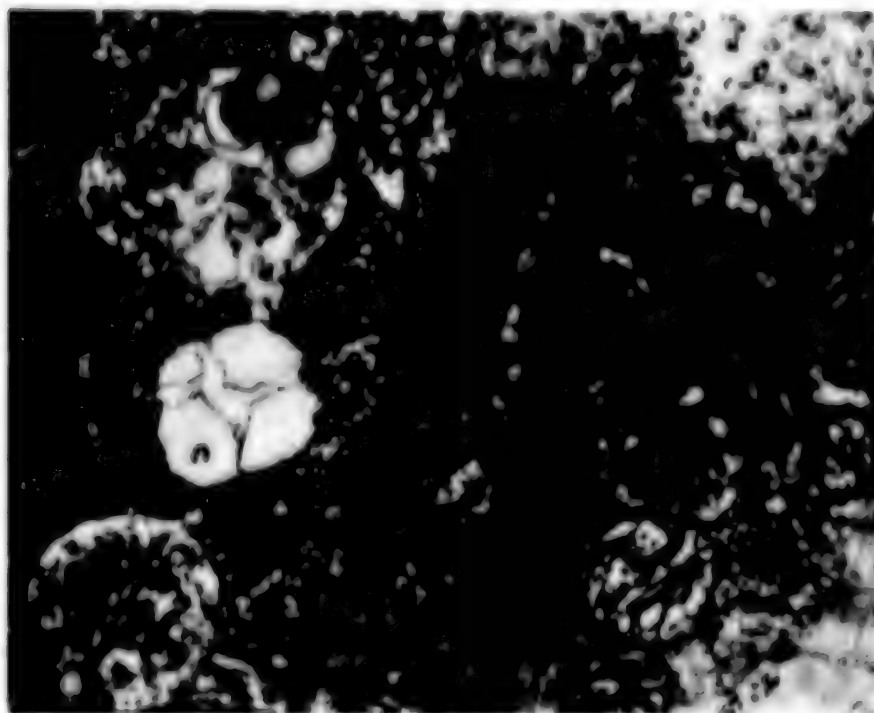


Figure 4. Autophagosomes containing remnants of myelin figures, some cristae and whole mitochondria in cardiomyocytes of rats decapitated 25 days after flight in weightlessness; magnification 16,000x

Thus, among the reported myocardial changes, the most prominent ones were microcirculatory disturbances, which cause development of tissular hypoxia when there is a greater load on the heart. However, these microcirculatory disturbances are not fatal, and they are transient, as is edema of cardiomyocytes, swelling of mitochondria and destruction of their cristae. This is indicated by restoration of ultrastructure of the myocardium of rats decapitated 25 days after the flight. The decrease in number of glycogen granules is, most probably, also related to the greater load on the heart with the return to earth's gravity and corresponding increase in energy expended by the heart.

It must be stated that weightlessness apparently also has an adverse effect on the condition of biological membranes, particularly those of the mitochondria and

sarcoplasmic reticulum. This is indicated by the numerous myelinoid elements of mitochondrial origin in animals submitted to weightlessness. We cannot rule out the possibility that appearance of myelinoid structures is related to destruction of some mitochondria due to decrease in energy requirements of the heart in weightlessness. This is also confirmed by the appearance of firm [dense] mitochondria and mitochondria with firm membranes.

We failed to demonstrate signs of atrophy, necrosis or lysis of cardiomyocytes in rats exposed to weightlessness. Nor did we find submicroscopic evidence of destruction and reorganization of contractile organelles of cardiomyocytes in such animals.

The cardiomyocytes of animals submitted to weightlessness during the flight contained many autophagosomes 25 days after landing, whereas only a few were present in other groups of rats. Such activation of the lysosome system could be related to appearance of myelinoid structures and elimination thereof from the cell or reutilization.

In summary, it may be assumed that AG prevents to a significant degree the development of ultrastructural myocardial changes, which appear under weightless conditions and when changing to earth's gravity, thus having some protective effect.

Evidently, the microcirculatory disorders appear at the time the animals change from weightlessness to earth's gravity, and they are acute. Only the appearance of the myelinoid structures can be referred to the consequences of long-term exposure to weightlessness.

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UDC: 629.78:612.751.1.015.3:577.152.313

PHOSPHATASE ACTIVITY OF RAT ANTEBRACHIAL BONES AFTER FLIGHT ABOARD THE COSMOS-936 BIOSATELLITE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981 pp 82-84

[Article by I. A. Popova and R. A. Tigranyan, submitted 10 Dec 79]

[English abstract from source] Activities of alkaline and acid phosphatases in ulnar and radial bones of rats flown for 18.5 days aboard Cosmos-936 and kept in a ground-based mockup were investigated. In both bones activity of acid phosphatase increased significantly and that of alkaline phosphatase decreased 6-10 hours postflight; in the synchronous experiment the only change was a decrease in the activity of alkaline phosphatase in the radius. An exposure of rats to artificial gravity did not normalize changes in phosphatase activities observed postflight. At R + 25 phosphatase activity in bones of flight rats returned to normal and even tended to exceed the control level in synchronous animals.

[Text] One can gain some idea about the intensity of mineralization and resorption processes in bone tissue by studying acid and alkaline phosphatase activity in this tissue [1, 2].

This study was conducted to evaluate the activity of acid (EC 3.1.3.2) and alkaline (EC 3.1.3.1) phosphatases in the radius and ulna of rats after flight aboard Cosmos-936 [1, 2].

Methods

This study was conducted on male Wistar SPF (Bratislava, CSSR) rats. The objective and conditions of experiments, as well as designations for animal groups, are described in [3].

Soft tissues were removed from the bones in question of the right and left antebrachium, then the bones were weighed, frozen in liquid nitrogen, and each bone was ground separately in a mortar. The powder was extracted for 3 min in a Potter homogenizer with 40 aliquots of 0.25 M saccharose, pH 7.4, containing 1 mM EDTA. After centrifugation of homogenates for 20 min at 3000 r/min, determination was made of acid [4] and alkaline [5] phosphatases in the supernatant according to rate of dissociation of h-nitrophenyl phosphate by optimized standard methods

using the beta of the Berlinger Firm (PRC). Enzyme activity was expressed in international units (IU) per mg protein. Protein was assayed by the method of Lowry [6].

All of the digital data were submitted to statistical processing with the use of Student's criterion ($P < 0.05$).

Results and Discussion

There was reliable increase in acid phosphatase activity, whereas alkaline phosphatase activity diminished reliably in both antebrachial bones of rats in the FW₁ [flight, weightlessness] group sacrificed 6-10 h after termination of the space flight (see Table). The observed changes in phosphatase activity of bone tissue warrant the assumption that the correlation between different reactions constituting the basis of processes of ossification and resorption of bone could be altered in the direction of prevalence of demineralization processes under the influence of space flight factors. Apparently, the weightlessness factor cannot play a decisive role, since changes in phosphatase activity were noted in rats of both the FW₁ and FC₁ [flight, centrifuge] groups.

Only a decline in alkaline phosphatase activity was observed in the radius and ulna of rats in the SW₁ [synchronous experiment, weightlessness] group sacrificed 6-10 h after termination of the ground-based synchronous experiment, and the changes were more marked in the SC₁ group exposed to increased gravity. At the same time, no differences were demonstrable in activity of acid phosphatase in bones of rats in the synchronous experiment and vivarium control [VC]. Evidently, the enzymatic reaction of alkaline hydrolysis of hexose phosphates, which are among the possible components of the system of formation of crystallization nuclei in the bone matrix, is quite sensitive to the effects of various nonspecific factors. This is also indicated by the results of testing phosphatase activity in animals in the C₁ [centrifuge] and C₂ groups, which presented some tendency toward decrease in alkaline phosphatase activity. Under the influence of this factor there was no change in acid phosphatase activity of antebrachial bones. In animals of the FW₁ group sacrificed on the 26th postflight day, acid and alkaline phosphatase activity of the bones did not differ from the levels obtained in the VC₁ group of rats. In flight group FC₂, activity of both phosphatases in the radius was close to the control level, whereas enzymatic activity of both phosphatases of the ulna was considerably higher than in the vivarium control. The time of restoration of normal correlation between mineralization and resorption processes is probably different for different bones, and apparently it is inversely related to the functional load on the bone. It may also be that the first stage of recovery is activation of mineralization, particularly its labile element, enzymatic dephosphorylation with the involvement of alkaline phosphatase.

It must be noted that there was significant increase in activity of both phosphatases on the 26th day after the ground-based synchronous experiment in the bones of rats of the SW₁ group, not only in comparison to the vivarium control, but the SW₁ group of the first stage of the experiment. This phenomenon may be based on several causes, the most probable of which is the regimen of exercise that could, in our opinion, be used at this stage of the functional tests. We previously demonstrated that there was an appreciable increase in acid and alkaline phosphatase activity in the bones [7] of rats conditioned in the mode of graded exercise (running on treadmill once a day for 7 days). If the expounded hypothesis is valid, the fact that the reaction of bone tissue to an exogenous factor, one of

the manifestations of which is its enzymatic activity, is not the same in rats in the synchronous ground-based experiment and the flight group merits attention.

Phosphatase activity in antebrachial bones (IU/mg protein)

Group	phosphatase	
	Alkaline	Acid
Ulna		
FW ₁ (9)	222.1 ± 16.1*	17.4 ± 1.54**
FC ₁ (8)	224.2 ± 27.0*	16.1 ± 0.93**
FW ₂ (10)	353.9 ± 36.3*	8.9 ± 0.95**
FC ₂ (10)	377.9 ± 25.4	11.9 ± 0.80*
SW ₁ (10)	243.1 ± 29.8	11.4 ± 0.73
SC ₁ (10)	217.6 ± 15.6*	9.9 ± 0.52
SW ₂ (10)	363.4 ± 19.0*	13.7 ± 0.51*
VC ₁ (10)	314.5 ± 24.4	11.1 ± 0.64
VC ₂ (10)	294.1 ± 21.5	8.7 ± 0.73
C ₁ (8)	202.3 ± 16.0*	12.9 ± 0.31
C ₂ (8)	329.8 ± 29.5	8.7 ± 0.76
Radius		
FW ₁ (10)	126.0 ± 19.3**	27.7 ± 2.35**
FC ₁ (8)	203.6 ± 47.4	24.5 ± 1.18**
FW ₂ (10)	293.2 ± 10.3**	10.6 ± 0.38**
FC ₂ (10)	343.2 ± 39.3	11.4 ± 0.75
SW ₁ (9)	193.2 ± 18.4*	15.8 ± 1.04
SC ₁ (10)	158.6 ± 13.2*	13.8 ± 0.35
SW ₂ (10)	396.7 ± 30.8*	20.8 ± 1.65*
VC ₁ (10)	285.2 ± 31.8	14.1 ± 1.36
VC ₂ (9)	260.1 ± 19.3	9.6 ± 0.39
C ₁ (8)	223.1 ± 30.5	15.2 ± 1.28
C ₂ (8)	272.9 ± 13.2	10.1 ± 0.96

Note: Number of cases is shown in parentheses. One and two asterisks signify values that differ reliably from those of the vivarium control and corresponding group in the ground-based synchronous experiment, respectively.

The aggregate of our findings indicates that there was a substantial change in acid and alkaline phosphatase activity in the antebrachial bones of rats as a result of an 18.5-day space flight, and this could have affected the correlation between intensity of mineralization and resorption processes in bone tissue. The reported changes are apparently the result of the complex effects of space flight factors. Creation of artificial gravity aboard the biosatellite did not correct entirely all of the changes in phosphatase activity in bones that were caused by space flight factors. There was complete restoration of phosphatase activity in rat antebrachial bone tissue 25 days after termination of the flight.

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CHEMICAL COMPOSITION OF MINERAL COMPONENT OF RABBIT BONES AS RELATED TO 30-DAY HYPOKINESIA

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981 pp 84-87

[Article by I. Ye. Didenko and A. I. Volozhin, submitted 1 Feb 79]

[English abstract from source] The study of the mineral component of bones of rabbits exposed to hypokinesia for 30 days demonstrated no changes in the Ca and P content or in the Ca/P ratio and revealed a decrease in the Mg, Na and K content. Possible involvement of bone tissue in the maintenance of electrolyte composition during prolonged hypokinesia is discussed.

[Text] Hypokinesia, as a factor that leads to changes in parameters of strength, which is one of the most important properties of the skeleton, is an important problem [1, 2]. At the same time, bone tissue is the site of deposition and active participant in regulation of electrolyte metabolism in the body [3, 4]. There are no data in the available literature concerning the "metabolic" function of skeletal bones with regard to electrolytes under hypokinetic conditions. At the same time, there are well-known facts indicative of changes in calcium, phosphorus and protein metabolism in mineralized tissues of animals during long-term hypokinesia [5-7]. Determination of the chemical composition of minerals of bone tissue, according to levels of Ca, P, Mg, Na and K under normal conditions and with restriction of motor activity, is one of the means of solving this problem. Moreover, it was interesting to study the effect of thyrocalcitonin (TCT) on mineral composition of bones during hypokinesia, since this is a hormone that has a normalizing effect on electrolyte metabolism during long-term immobilization [8-10].

Methods

Experiments were conducted on 65 chinchilla rabbits initially weighing 2500±220 g. The animals were divided into 4 groups: the first group consisted of control animals (23 rabbits); the second of 13 animals kept under hypokinetic conditions; the third was a control group (13 animals) given TCT; the fourth consisted of animals given TCT (16 rabbits) during hypokinesia. The rabbits were put in special cages with movable walls to create hypokinesia. The size of the cage could be adjusted to conform with the size of the animal. Control rabbits were kept in standard vivarium cages (one animal in each).

The animals were given pellet feed with a supplement of hay, cabbage and carrots. Water intake was not restricted. A preparation of bovine TCT diluted in distilled

water was injected hypodermically twice a day (morning and evening) at the rate of 30 MRC units* of hormone per day per rabbit.

After termination of the experiment, the rabbits were sacrificed by producing an air embolism; the humerus, scapula, femur, calcaneus, second vertebra and mandible were removed. The soft tissues were removed from the bones; they were then dried and ashed in a muffle furnace at 500°C for 5 h. Concentrations in ash were determined with a type FPL-1 flame photometer using the conventional modified method [11]. Ca and Mg content was determined with an atomic absorptiometer, P by spectrophotometry on an SF-4A spectrophotometer.

In addition, we determined the correlation between levels of different elements and Ca/P, Na/K, Na/Ca, K/Ca and Mg/Ca ratios. All of the data were submitted to processing by the method of variational statistics.

Results and Discussion

Ca content of mineral component of different bones of control rabbits was notable for great stability, constituting 38.17 to 42.1 g/100 g ash (see Table). There was even less fluctuation of P content, while Ca/p ratio was minimal in the femur and maximal in the vertebra and humerus. The differences in Ca/P apparently reflect the individual rate of reorganization of bones and amount of spongy and compact substance [6]. There was no correlation between Ca and P content.

Mg content was 695 mg/100 g ash in the humerus, 740 in the femur, 716 in the scapula, 859 in the calcaneus, 786 in the vertebra and 838 mg in the mandible. Thus, the Mg level fluctuated over a wider range than Ca and P. It should also be noted that there was a higher concentration of Mg in bones containing a large amount of spongy substance than in lamellar and tubular bones, in which there was prevalence of compact tissue.

The ratio between Mg and the most stable mineral component, Ca, was rather stable in various bones, ranging from 0.0180 to 0.188, and only in the mandible did it constitute 0.0209. We failed to demonstrate a reliable correlation between Ca and Mg content of bones.

Na concentration constituted 534-599 mg/100 g ash in tubular bones and the scapula, 437-484 mg in the calcaneus and mandible, and only 348 mg in the vertebra.

A similar pattern was demonstrated in K, the concentration of which constituted 53-67 mg/100 g ash in tubular bones, 41 in the scapula, 28.5 in the mandible, and considerably lower in the calcaneus and vertebra.

A reliable positive correlation was demonstrated between K and Na ($P < 0.05$) only in tissues with less than 50 mg/100 g ash of K, i.e., in all but the tubular bones. K/Ca and Na/K depended primarily on the concentration of K in mineralized tissues, since the Na and Ca levels were more stable in different bones.

*The standard was developed in 1965 in the Department of Biological Standards of the London National Institute of Medical Research.

Chemical composition of mineral component of rabbit bones (per 100 g ash) under normal and hypokinetic conditions, and with administration of thyrocalcitonin

Bone	Group	Levels of elements									
		K		P		Mg		Na		I	
		g	%	g	%	mg	%	mg	%	mg	%
Humerus	1	38.8 ± 2.5	100	17.9 ± 0.78	100	69.6 ± 50.9	100	549.6 ± 10.6	100	62.3 ± 8.1	100
	2	37.9 ± 1.5	97.7	18.3 ± 1.1	102.2	772.7 ± 91.4	111.9	563.4 ± 55.8	91.9	69.5 ± 5.5	73.6*
	3	38.9 ± 1.4	100.3	17.9 ± 0.5	100.0	749.6 ± 61.0	107.8	593.8 ± 53.8	99.0	64.3 ± 11.5	95.5
	4	38.3 ± 1.9	98.7	17.9 ± 1.2	100.0	751.1 ± 72.4	108.5	580.7 ± 61.8	98.3	57.6 ± 16.8	85.6
Femur	1	41.3 ± 2.1	100	19.5 ± 2.1	100	740.5 ± 62.7	100	567.0 ± 47.1	100	53.2 ± 10.2	100
	2	42.8 ± 1.2	103.6	17.8 ± 0.8	91.3	771.9 ± 110.7	104.2	577.3 ± 50.6	101.8	47.8 ± 14.3	89.8
	3	40.8 ± 2.6	98.8	17.9 ± 0.6	91.8	779.7 ± 71.5	105.3	584.5 ± 29.5	104.0	51.0 ± 15.2	95.8
	4	41.6 ± 1.9	100.7	18.2 ± 0.9	93.3	724.2 ± 76.9	97.8	588.9 ± 63.6	102.1	42.5 ± 8.6	79.8
Scapula	1	41.2 ± 2.7	100	17.8 ± 1.2	100	716.0 ± 68.9	100	534.0 ± 34.8	100	41.0 ± 7.2	100
	2	42.2 ± 1.9	102.4	17.4 ± 0.9	97.8	702.9 ± 68.7	98.2	457.2 ± 47.6	85.6	20.6 ± 6.8	50.2*
	3	42.2 ± 3.7	102.4	17.3 ± 1.2	97.2	732.2 ± 74.6	102.3	566.5 ± 85.6	106.1	35.9 ± 14	87.6
	4	40.7 ± 2.7	98.8	17.3 ± 0.9	97.2	711.3 ± 73.3	99.3	513.5 ± 78.0	96.2	27.8 ± 6.6	67.8
Calcaneus	1	41.9 ± 1.8	100	18.0 ± 0.97	100	858.6 ± 30.2	100	483.8 ± 63.5	100	12.3 ± 2.8	100
	2	40.4 ± 1.6	96.4	17.7 ± 0.3	98.3	757.6 ± 48.3	88.2*	479.0 ± 75.7	90.7	12.0 ± 2.6	97.6
	3	40.1 ± 2.0	96.4	17.6 ± 0.6	97.8	777.9 ± 98.3	90.6	529.5 ± 39.2	109.2	14.2 ± 1.9	115.4
	4	40.2 ± 3.5	95.9	17.4 ± 1.3	96.7	720.2 ± 56.3	83.9*	473.5 ± 80.8	97.9	12.9 ± 1.7	104.8
Vertebra	1	42.1 ± 2.0	100	17.9 ± 0.5	100	786.5 ± 85.2	100	348.4 ± 79.2	100	11.4 ± 4.7	100
	2	43.5 ± 3.1	103.3	18.1 ± 0.3	101.1	704.8 ± 34.6	89.6	322.8 ± 84.8	92.7	10.6 ± 2.6	93.0
	3	43.0 ± 2.2	102.1	17.9 ± 0.4	100.0	749.7 ± 82.8	95.3	329.2 ± 94.3	91.9	10.8 ± 8.0	94.7
	4	42.2 ± 1.3	100.2	18.1 ± 0.7	101.1	746.4 ± 65.0	94.6	317.3 ± 62.1	91.0	12.1 ± 2.5	106.1
Mandible	1	40.1 ± 0.8	100	17.4 ± 0.5	100	838.3 ± 38.6	100	437.4 ± 27.3	100	28.5 ± 2.8	100
	2	39.9 ± 0.8	99.5	17.3 ± 1.0	99.4	817.8 ± 29.7	97.6	449.9 ± 26.1	102.9	26.2 ± 4.3	91.9
	3	40.7 ± 1.2	101.5	16.9 ± 0.4	97.1	828.0 ± 37.3	98.7	455.8 ± 13.3	104.2	23.5 ± 2.2	82.5
	4	40.6 ± 0.6	101.2	17.2 ± 0.98	98.9	840.2 ± 40.0	100.2	452.6 ± 12.2	103.5	25.5 ± 1.2	89.5

* $P < 0.05$.

The obtained data indicate that Ca and P are the most stable mineral components of bones, while the levels of such elements as Mg, Na and, especially, K fluctuate over wider ranges. The latter is apparently attributable to the distinctions of the crystalline phase of different bones and ground substance causing binding of Mg, Na and K.

The results of our studies confirm the opinion that bone is the organ of deposition not only of Ca and P, but other elements [7].

It is known [10] that there are substantial changes in electrolyte metabolism of rabbits during 30-day hypokinesia. In interpreting this effect, one must also take into consideration the role of the bone system in regulating the stability of Ca, P, Mg, Na and K concentrations in body fluids.

According to the obtained data, 30-day hypokinesia did not lead to changes in Ca, P or Ca:P in rabbit skeletal bones. Consequently, the reduction of body mass demonstrated in this experiment and reported in an earlier publication [9] is manifested against the background of normal levels of the main components of the mineral phase of bones.

There was negligible increase in concentration of Mg in the humerus and femur during hypokinesia, whereas it presented a distinct tendency toward decrease in other bones. Na content dropped in all bones with the exception of the femur and mandible. An analogous direction of changes was demonstrated in concentration of K in the bones of hypokinetic rabbits.

Correlation analysis revealed a reliable positive correlation between concentrations of K and Na in the same bones of rabbits in the first and second groups. There was an analogous correlation between P and K content of the vertebra, mandible and scapula ($r = 0.60-0.82$). Such a correlation was demonstrated only in the calcaneus of the rabbits in the first group. These data can be explained by assuming, for example, that there is a compound containing K and P in bone tissue. Perhaps, the amount of this compound in bones increases under hypokinetic conditions.

It was found that the high positive coefficient of correlation between K and P of the mandible and vertebra was associated with an equally high, but negative correlation between Na and P ($r = 0.73-0.77$).

Administration of TCT to rabbits whose movements were not restricted did not alter the concentrations of Ca and P in bone ash. There was some elevation of Mg level in tubular bones and the scapula, with a tendency toward decline in other mineralized bones. There were no consistent changes in Na and K content.

The changes referable to chemical composition, which were attributable to hypokinesia, were generally somewhat less marked in the fourth group of rabbits than in the second.

A previously published study [10], which was conducted on the same animals, established that there was a decrease in blood plasma Ca concentration and increased excretion thereof in urine and feces of rabbits as a result of 30-day hypokinesia. This was not associated with changes in concentration of K and Na in blood, in spite of increased excretion of these elements from the body. A comparison of

these data to those obtained in the present study suggests that the mechanism of redeposition of electrolytes in bone tissue plays a part in preserving the normal levels of Na and K in blood under hypokinetic conditions.

The fact that there is no change in Ca content of bones under hypokinetic conditions, in spite of significant increase in excretion thereof, merits attention. This is attributable to the fact that, in growing animals, inhibition of bone reorganization under hypokinetic conditions leads to reduction of overall skeletal mass without significant changes in crystalline structure of mineral substance.

The diminished utilization of Ca in the process of building bone tissue in experimental animals is apparently the prime cause of increased excretion of this element by rabbits in the course of 30-day hypokinesia.

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EFFECT OF HYPERBARIC NITROGEN AND OXYGEN ATMOSPHERE ON ACTIVITY OF RESPIRATORY CENTER

MOSCOW KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
pp 88-89

[Article by I. S. Breslav, N. Z. Klyuyeva and G. V. Troshikhin, submitted 28 Nov 79]

[English abstract from source] In anesthetized cats inspiratory activity of the respiratory center at first increased and then decreased with increases in total pressure of the nitrogen-oxygen atmosphere 11, 11 and 21 atm (at normal PO_2). The effort made by respiratory muscles increased gradually. These changes were augmented by hypercapnia. Possible role of nitrogen anesthesia and compensatory reactions to the increased breathing resistance in the development of the above changes is discussed.

[Text] Man's exploration of the oceans puts a number of problems to physiology. One of them is the increased resistance to an aquanaut's breathing, since he has to breathe with mixtures under elevated pressure and, consequently, with increasing density, as he submerges, and this could seriously limit vital functions [1-3]. The density of the environment [atmosphere] can be reduced significantly by using helium and oxygen gas mixtures. However, in a number of cases, it is desirable to use mixtures containing nitrogen. At high pressures, in addition to relatively greater density, this gas has a marked anesthetic effect [4].

We cannot rule out the possibility that the anesthetic [narcotic] effect of high partial nitrogen pressure (P_{N_2}) can extend to the respiratory center and disrupt compensatory reactions to the higher resistance to the flow of gases in the airways. Development of such a vicious circle presents the danger of decompensation of the aquanaut's respiratory function, with all the ensuing consequences. True, some authors tend to deny the depressing effect of a high P_{N_2} on regulation of respiration [5], but thus far without any serious enough evidence.

The lack of direct data concerning the activity of the respiratory center under hyperbaric conditions in general and with high P_{N_2} in particular is a hindrance to the solution of this problem. Our objective here was to fill, at least in part, this gap.

Methods

This study was conducted on 15 tracheostomied cats under mild urethane and chloralose anesthesia. The animals, which were immobilized in a special stand, were

put in a pressure chamber, where excess pressure of the nitrogen-oxygen mixture constituted 6, 10 and 20 kgf/cm², with retention of normal partial oxygen pressure (0.21 kgf/cm²). The density of the atmosphere was increased by 7, 11 and 21 times, respectively, as compared to ordinary air at sea level, while P_{N₂} was increased to 5.8, 9.8 and 19.8 kgf/cm². Total exposure of the animals at each "depth" lasted 10 min. Readings were taken in the 3d min of exposure at the tested pressure for 1 min, after which the readings were repeated under hypercapnic conditions, i.e., for 2 min while breathing with a carbon dioxide enriched mixture (P_{CO₂} 50 mm Hg at all of the tested pressures), from a bag situated in the chamber. In all, inhalation of the hypercapnic mixture lasted 3 min.

We used integrated activity of diaphragmatic neurons (ADN), recorded by a previously described method [6], as an indicator of the functional state of the respiratory center. The fluctuations of intrathoracic pressure (ITP), measured through an esophageal catheter and converted into an electric signal, served as the gage of overall exertion developed by respiratory muscles. The respiratory volume (V_T), which was recorded by pneumotachography, served as an indicator of performance of this exertion: A Fleisch tube equipped with a strain gage was connected to the tracheal cannula. The measuring and recording equipment was outside the chamber, being equipped with plugs to connect it to the sensors.

Results and Discussion

As shown in Table 1, at a pressure of 7 kgf/cm², ADN increased somewhat, as compared to the control (air at normal pressure). However, further elevation of ambient pressure was associated with a decline of ADN, rather than rise. ITP rose at a pressure of kgf/cm², considerably more than ADN and, unlike the latter, continued to rise drastically at pressures of 11 and 21 kgf/cm². V_T increased slightly up to 11 kgf/cm², and did not change any more at a pressure of 21 kgf/cm².

Table 1. Respiratory parameters as related to different ambient pressure (M±m)

Pressure, kgf/cm ²	ADN, relat. units	ITP, mm water	V _T , ml
1 (control)	41.2±4.8	9.7±1.6	34.1±2.8
7	46.0±4.6	15.2±2.3	36.1±3.8
11	40.1±7.0	22.7±3.4	40.6±3.4
21	35.6±6.0	30.0±4.6	40.2±5.2

There were the same tendencies, but more marked, under hypercapnic conditions (Table 2).

ADN increased somewhat at a pressure of 7 kgf/cm², then dropped, while ITP gradually rose with increase in pressure, as it did under normocapnic conditions. V_T increased up to a pressure of 11 kgf/cm², and showed virtually no change at 21 kgf/cm².

Table 2. Respiratory parameters under hypercapnic conditions (P_{ICO_2} 50 mm Hg) at different ambient pressure (M±m)

Pressure, kgf/cm ²	ADN, relat. units	ITP, mm water	V_T , ml
1 (control)	51.5±6.4	13.7±1.8	49.5±4.0
7	58.0±6.8	23.9±4.6	57.1±5.1
11	47.8±6.8	30.1±7.4	60.5±7.1
21	42.2±7.0	36.8±6.8	56.0±10.3

Thus, there was some increase in activity of the respiratory center with moderate increase in atmospheric pressure. We previously succeeded in demonstrating that resistance to the flow of inhaled gas or using a respiratory gas mixture of high density ($\text{SF}_6\text{-O}_2$) elicits activation of diaphragmatic [phrenic] motoneurons of cats due to attenuation of inspiratory inhibition as a result of diminished stimulation of receptors of expansion of the lungs [6, 7]. However, the overall exertion developed by respiratory muscles increased considerably more than ADN, which is indicative of involvement of some other mechanisms as well in the compensatory reaction to increased resistance to breathing. These mechanisms may be reflexes from receptors of intercostal muscles, or the property of muscle fibers to increase the strength of contractions in response to expansion [8]. These mechanisms continued to function with the highest pressure that we tested. Evidently, expressly they held the respiratory volume at a level that differed little from the control, whereas activity of the respiratory center (measured by the value of ADN) already began to drop at higher pressures of the environment.

What is the cause of the demonstrated depression of the central system of regulation of respiration in the presence of severe hyperbaria? The anesthetic effect of nitrogen could be involved, and it should have been present at the tested levels of its partial pressure [9]. In this case, manifestation of this effect was probably aided by the urethane-chloralose anesthesia that we used. It is not surprising that depression of the respiratory center was particularly noticeable in the presence of hypercapnia: as we know, CO_2 enhances the anesthetic effect of nitrogen [10].

The evidence obtained for the first time of both the stimulating and depressing effects of hyperbaria on different elements of the system of control of respiration is, in our opinion, of both theoretical and practical interest, and it requires further experimental investigation.

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BRIEF REPORTS

UDC: 629.78.048.4:(612.2+612.121.2

COMPARATIVE STUDY OF RESPIRATORY FUNCTION AND ACID-BASE EQUILIBRIUM OF MAN WITH CHANGES IN GAS ATMOSPHERE AND MICROCLIMATE OF PRESSURE CHAMBER

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981 pp 90-92

[Article by V. V. Zhuravlev, submitted 28 Feb 80]

[Text] In the last few years, increasing attention is being given to the question of the combined effect on man of altered gas composition and microclimate of the ambient environment. When the gas composition of the air environment changes, first to react are the body systems related to transport of oxygen and carbon dioxide [1-4]. Our objective here was to study the degree of change in respiratory function and acid-base balance (ABB) in human blood with increasing hypercapnia and relative hypoxia under different microclimate conditions in a pressurized chamber.

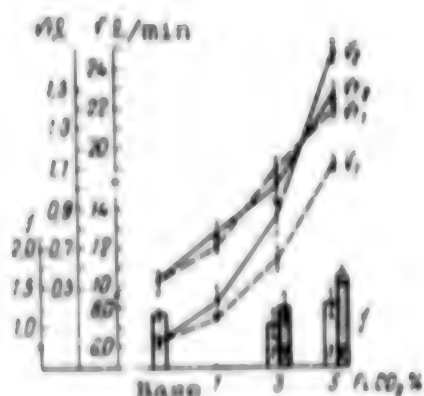
Methods

We conducted 2 series of studies in a pressure chamber with the participation of 14 male volunteers 24-36 years of age. CO_2 content of inhaled air (FiCO_2) increased from 0.05 to 5%, while O_2 concentration (FiO_2) decreased from 22 to 17% at the rate of 1% per 4-8 h as a result of the subjects' vital functions. The studies were conducted when FiCO_2 reached 1, 3 and 5% (Table 1, 1st-3d phases).

We conducted a total of 121 tests, 33 of which were referable to the initial and recovery periods. Respiration was tested by the Douglas method. An MMC-7 oxymeter and Godart capnograph were used to analyze the air. ABB was determined on an Astrup apparatus. The subjects received a standard diet constituting 3200 kcal/day. We conducted the study with the subjects in a state of relative rest.

Results and Discussion

With increase of FiCO_2 there was a reliable increase in pulmonary ventilation ($\dot{V}$) in both series of studies (see Figure). Under optimum microclimate conditions the increase of $\dot{V}$ first occurred due to increase in tidal volume ($\dot{V}_T$), whereas with 5% FiCO_2 there was also faster respiration (f). In the presence of hyperthermia the increase in pulmonary ventilation occurred both due to increase in $\dot{V}_T$ and faster respiration starting at 3% FiCO_2 . The differences in pulmonary ventilation between series of studies with 1 and 3% FiCO_2 are unreliable, which is consistent with the data of other authors [5]. With 5% FiCO_2 , tidal volume was reliably higher in the second series than the first.



Changes in minute volume ($\dot{V}$), tidal volume ($\dot{V}_T$) and respiratory rate (f) as a function of F_{ICO_2} (1) and combination thereof with hyperthermia (2)

Output of oxygen ($\dot{V}O_2$) and carbon dioxide ($\dot{V}CO_2$) showed virtually no change in all studies, with the exception of the last phase (Table 2). With 5% F_{ICO_2} there was a reliable increase in $\dot{V}O_2$ and $\dot{V}CO_2$, the degree of change in both being unrelated to the microclimate.

The respiratory quotient (R) did not change appreciably in any of the tests, and it declined (to 0.68 and 0.77, respectively) with 5% F_{ICO_2} in both series, which could be indicative of relative retention of carbon dioxide in the body. Retention of carbon dioxide is confirmed by the dynamics of levels thereof in alveolar air (F_{ACO_2}).

Table 1. Experimental conditions

Parameter	Base data	Series					
		I			II		
		phase					
		1	2	3	1	2	3
FiO ₂ , %	22	21±0.5	19±0.5	17±0.5	21±0.5	19±0.5	17±0.5
FiCO ₂ , %	0.05	1±0.2	3±0.2	5±0.2	1±0.2	3±0.2	5±0.2
Air temp., °C	21.5±1	20±2.0	20±2.0	20±2.0	33±2.0	33±2.0	33±2.0
Air humidity, %	5-10	50±15	50±15	50±15	90±5.0	90±5.0	90±5.0

Table 2. Parameters of respiration, M $\pm$ m

Phase	Series	$\dot{V}O_2$, ml/min	$\dot{V}CO_2$, ml/min	R	$\dot{V}_E$	Q_{AO_2} , ml/min	$Q_{\text{AO}_2}, \dot{V}O_2$	$F_{\text{ACO}_2}, \%$
I	Base data	271.4 ± 19.7	211.1 ± 11.2	0.78 ± 0.007	2.33 ± 0.09	241.3 ± 42.5	5.12 ± 0.12	5.71 ± 0.09
	I	300.7 ± 11.4	240.1 ± 10.4	0.8 ± 0.09	2.81 ± 0.07	271.3 ± 28.8	5.04 ± 0.1	5.48 ± 0.08
	II	267.2 ± 19.7	241.0 ± 14.2	0.91 ± 0.09	2.89 ± 0.21	$1163 \pm 153.7^*$	$4.9 \pm 0.19^*$	5.3 ± 0.18
II	I	287.5 ± 33.9	229.4 ± 29.9	0.79 ± 0.1	$1.44 \pm 0.47^*$	$1262 \pm 77.1^*$	$4.9 \pm 0.14^*$	6.07 ± 0.18
	II	335.7 ± 23.7	287.2 ± 22.8	0.86 ± 0.09	$4.03 \pm 0.21^*$	$1595 \pm 37.1^*$	$4.62 \pm 1.02^*$	$6.17 \pm 0.16^*$
III	I	451.7 ± 10.3	$305.5 \pm 10.7^*$	$0.68 \pm 0.1^*$	$4.21 \pm 0.34^*$	$2247 \pm 30.4^*$	$1.93 \pm 0.04^*$	$6.62 \pm 0.04^*$
	II	424.1 ± 21.3	$331.7 \pm 8.7^*$	$0.77 \pm 0.9^*$	$5.79 \pm 0.51^*$	$2081 \pm 818.4^*$	$0.98 \pm 0.01^*$	$6.9 \pm 0.13^*$

*Statistically reliable differences between series for mean values.

With change in F_{ICO_2} and F_{IO_2} , the rate of delivery of oxygen to the alveoli (Q_{AO_2}) increased, and starting with the second phase of the tests, Q_{AO_2} was reliably greater in the second series than the first. Respiratory efficiency

($\dot{Q}_{A,O_2}/\dot{V}O_2$) diminished. Concurrently with diminished efficiency, there was also worsening of economy of respiration, an indicator of which was increase in value of respiratory equivalent (VE). The decrease in efficiency and economy was reliably greater at the last phase of the tests in the series with hyperthermia.

Examination of blood ABB revealed that, under hyperthermic conditions, there was development of acidemia with increase of FICO_2 (Table 3). Such ABB disturbances had been previously described with 8-15% FICO_2 under normal microclimate conditions.

Table 3. Changes in blood ABB of subjects under the influence of hypercapnia and hyperthermia

Subject	FICO_2 , %	pH	PaCO_2 , mm Hg	BB, meq/l	BBC, meq/l	SB, meq/l	Blood oxygenation, %	pO_2 , mm Hg
D-v		7.39	49.0	55.0	-2.5	36.0	97.2	28.3
B-n	3	7.36	52.0	52.0	-2.0	35.5	97.3	28.7
D-v		7.34	53.0	52.5	-4.5	28.0	96.5	30.8
B-n	5	7.39	54.0	55.0	-6.0	29.0	96.1	32.4

Key: BB) buffer bases BBC) buffer base change SB) standard bicarbonates

These results revealed that ambient microclimate is also important to man's tolerance of an altered gas composition of air, in the presence of the same concentrations of oxygen and carbon dioxide in inhaled air. Thus, in our studies with addition of hyperthermia, there was a change in respiratory function and, first of all, an increase in pulmonary ventilation. We cannot rule out the possibility that the more marked changes in respiration in this case are based on the observed acidotic changes in ABB, as well as hyperthermia, which elicited a change in the same direction in the curve of dissociation of blood oxyhemoglobin [6, 7]. The presence of a high concentration of carbon dioxide in inhaled air (5%) prevents compensation of developing acidosis solely by intensification of breathing, and for this reason the body moves to another functional level with high CO_2 content. In this case, this is aided by attenuation of the "Haldane effect," as a result of reduced concentration of air in inhaled air [8].

Most researchers believe that hypercapnia reduces metabolic processes and, consequently, oxygen uptake [5, 9, 10]. This fact was not corroborated here. In almost all of the tests we observed an increase in oxygen uptake, which was particularly marked with 5% carbon dioxide and 17% oxygen in inhaled air. Comparable results were obtained by N. A. Agadzhanian et al. [11, 12]. The combination of hypercapnia and relative hypoxia, as well as the other factors inherent in situations where man spends a long time in a pressure chamber (including the emotional background) prevent a decrease in metabolism.

Thus, these series of tests involving the use of an altered gas environment, as well as the complex effects of altered gas environment and hyperthermia, yielded data indicative of significant adaptive changes in the subjects. It was demonstrated that hyperthermia in the presence of 5% CO_2 in inhaled air elicited more profound changes in respiratory function and ABB. This was manifested by a greater increase in minute volume of respiration, as well as decrease in economy and effectiveness of respiration, as indicated by elevation of VE and QA parameters.

It should be noted that there was an increase in oxygen uptake and carbon dioxide output with increase in hypercapnia in both series of tests.

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EFFECTS OF SOME PHARMACOLOGICAL AGENTS AND DIFFERENT LEVELS OF ILLUMINATION ON HUMAN PERFORMANCE

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981 pp 92-93

[Article by R. I. Bogatova, V. N. Chernyakova and T. N. Soboleva, submitted 31 Jan 80]

[Text] Our objective was to test the influence of different modes of illumination and psychotropic pharmacological agents on man's mental performance.

Methods

We used a mockup of a Soyuz type spacecraft in our studies. Mental performance ["fitness for work"] was tested with the tables of Anfimov. The data were processed by the method of V. I. Agarkov [1], which yields an overall indicator of mental performance, which synthesizes its main parameters--productivity and efficiency. There were no practice sessions with the subjects using this method, since the interval between studies usually constituted 10 days for each of them.

In order to regulate the functional state of the subjects, they took increasing doses of phenamine (from 0.001 to 0.016 g, daily dosage 0.032 g), fenibut and fepiron (0.05 to 0.8 g, daily dosage 1.6 g) or combinations thereof every 30 min.

The cancellation test was conducted under three illumination conditions, the levels of which were measured in the plane of the work zone with a lux meter. In the first mode, illumination constituted 58 lux (fluorescent lights and filament lamp--one of the lights used by reporters [?]); in the second mode it was 32 lux (fluorescent lights alone) and in the third mode 140 lux (3 "reporter" lights and fluorescent ones).

Two series of tests were conducted involving 12 subjects 23 to 40 years of age. In the first series (96 tests), the cancellation test was performed in the three modes of illumination without drugs and in the second (96 tests) with intake of phenamine, fenibut and fepiron, as well as combination of phenamine with fenibut or fepiron in the first mode, intake of fenibut and fepiron in the second mode, intake of fenibut, fepiron, phenamine and combinations of phenamine with fenibut or fepiron in the third mode of illumination.

With all modes of light, in the second series the subjects were given placebo, and the results of the cancellation test in this variant were interpreted as a control for the results obtained after intake of drugs.

All of the data were submitted to statistical processing by the method of Fisher and Student.

Results and Discussion

Performance level constituted 233.2 ± 8.56 with the first illumination mode. Analysis of the data with an altered mode of illumination revealed that performance was lower with less light (217.1 ± 12.06 ; $P = 0.1$) and was virtually the same as in the first mode when illumination was increased (231.6 ± 13.03 ; $P = 0.9$).

Fenibut did not have an optimizing effect on quality and level of performance of the cancellation test; fepiron and phenamine with fenibut increased efficiency appreciably.

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STUDY OF INDIVIDUAL DISTINCTIONS IN HUMAN PERFORMANCE AS RELATED TO LENGTHY MEDICAL EXAMINATIONS

Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981 pp 93-95

[Article by V. N. Chernyakova and V. S. Dyundina, submitted 28 Jan 79]

[Text] When studying operator performance as it relates to the tasks and conditions of space flights, it is very important to consider individual distinctions of performance of each operator when analyzing results obtained from studies involving a small number of subjects. To detect these distinctions, it is necessary to observe beforehand the productivity of the subjects in some selected form of work and dynamics thereof over a long period of time. The cancellation test can be used for this purpose [1]. The link established by a number of authors between a man's general functional state, his efficiency [fitness for work] and state of the body's circadian system [2-4] justifies analysis of the distinctions of daily biorhythms and evaluation of their influence on efficiency. In addition to demonstration of individual distinctions, such analysis could, to some extent, help predict the subjects' performance.

Methods

Two essentially healthy men stayed in an isolated room for half the work day, and in it they performed a 10-min cancellation test, according to which the subjects' attention was evaluated, in addition to other examinations. We took into consideration the number of symbols scanned (productivity), number of mistakes and productivity with consideration of mistakes (overall productivity). The studies did not disrupt the established work, rest and sleep schedule of each subject. They were conducted for 3 days in a row at intervals of 3 weeks. In all, there were 5 cycles of tests with one subject (B) and 4 with the other (N).

During the 3-day examination, we recorded several physiological parameters (heart rate, body temperature, diuresis, rate of excretion of sodium and potassium in urine) at 0300, 0700, 1100, 1500, 1900 and 2300 hours, and they were used to plot the curves of circadian rhythms. In order to demonstrate individual distinctions of rhythms, for each subject we plotted a chart of the phases, calculated the mean values of level, amplitude, maximum and minimum over the period of the study. When analyzing the circadian rhythms, we took into consideration the shape of the daily curves and stability of phase position.

The t criterion of Student was used to determine the reliability of differences between the parameters analyzed.

Results and Discussion

The data listed in Table 1 were obtained as a result of the studies using cancellation tests. They indicate that the attention span evaluated by this test was not the same in the two subjects. Thus, it was substantially lower in subject B. than N. The difference in overall productivity was determined primarily by the fact that subject B. made considerably more (almost twice as many) mistakes than subject N. In addition, B. worked somewhat slower than N.

Table 1. Results of cancellation test

Cycle	Subject					
	B.			N.		
	S	n	A	S	n	A
First	1725	17.8	885	2310	6.5	1845
Second	1937	15.7	1232	2385	11.0	1890
Third	2070	16.5	1328	2325	3.3	2175
Fourth	2484	22.0	1471	2213	10.0	1783
Fifth	2595	11.3	2085			

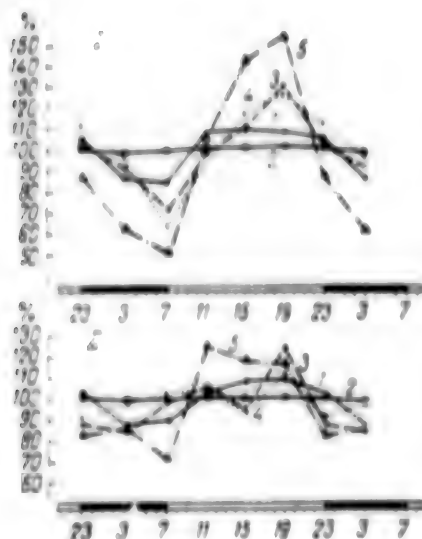
Key: S) productivity
 A) productivity with consideration of mistakes
 n) number of mistakes

Table 2. Characteristics of circadian rhythms of physiological functions studied

Parameter	Level	Amplitude	Maximum, value	Maxim. time	Minimum, value	Minim., time
Subject B.						
Heart rate/min	66.1 ± 0.66	11.1 ± 1.05	77.3 ± 1.39	15	55.0 ± 0.72	7
Body temperature, °C	36.19 ± 0.03	0.38 ± 0.02	36.58 ± 0.03	19	35.55 ± 0.06	3
Diuresis, ml/min	0.60 ± 0.07	0.51 ± 0.10	1.31 ± 0.17	19	0.47 ± 0.03	7
Sodium excretion, meq/min	105.2 ± 9.19	60.1 ± 11.7	165.3 ± 18.3	19	52.5 ± 6.9	7
Potassium excretion, meq/min	34.0 ± 1.95	23.0 ± 1.72	56.9 ± 3.04	19	11.9 ± 1.45	7
Subject N.						
Heart rate/min	61.7 ± 0.82	8.6 ± 0.91	74.2 ± 1.61	19	57.0 ± 0.43	3
Body temperature, °C	36.12 ± 0.06	0.18 ± 0.04	36.49 ± 0.06	11	36.11 ± 0.09	3
Diuresis, ml/min	0.66 ± 0.03	0.31 ± 0.05	0.97 ± 0.07	19	0.43 ± 0.03	3
Sodium excretion, meq/min	92.2 ± 5.95	50.3 ± 7.88	142.4 ± 12.1	19	54.5 ± 7.10	23
Potassium excretion, meq/min	26.2 ± 2.02	14.5 ± 1.67	40.6 ± 3.03	11	12.3 ± 1.57	7

Analysis of the dynamics of productivity in the cancellation test, as compared to the distinctions of circadian rhythms revealed that the plotted phase charts [5] and results of analysis of some parameters of circadian rhythms of physiological functions studied (see Figure and Table 2) enable us to detect the subjects individual distinctions. The rhythms of subject B. have one peak, they are characterized by a high amplitude, with the maximum point for 4 out of 5

of the circadian curves referable to 1900 hours and the minimum to 0700 h. The rhythms of subject N. had a lower amplitude, presenting one or two peaks, with a wider scatter of maximum and minimum points than in B.



Charts of phases of subjects B. (I) and N. (II). X-axis, time of day; y-axis, parameters (% of mean 24-h value). White rectangles refer to sleep period and black to waking (arbitrarily)

- 1) heart rate per min
- 2) body temperature, °C
- 3) diuresis, ml/min
- 4) sodium excretion (meq/min)
- 5) potassium excretion (meq/min)

On the eve of the third cycle of tests, the waking-sleep cycle of the subjects was unexpectedly interrupted. As a result, there was a decline in amplitude of some circadian rhythms, appearance of additional peaks on the curves, with shifting in different directions of maximum and minimum points. These changes were more appreciable in subject B. than N., and they persisted for a longer time, since some were noted in the fourth cycle.

In the course of the study there was gradual increase in productivity of subject B. in the cancellation test. While the increment was not uniform, its lowest values were noted in the third cycle, i.e., when the circadian rhythms were disrupted. In subject N., overall productivity gradually increased during the first three cycles. The negligible deviations of circadian rhythm that were noted did not cause it to diminish.

Thus, the initial structure of the circadian system (subject B.) was impaired as a result of disruption of the sleep-waking schedule, and this was associated with deterioration of efficiency according to the cancellation test. Consequently, it may be assumed that a subject's performance with such organization of the circadian system is more subject to change with disruption of sleep-waking schedule. The different results obtained with the cancellation test, differences in phase and amplitude structure of circadian rhythms and individual reaction to disruption of sleep-wakefulness rhythm are the distinctions that it is expedient to consider when forecasting the fitness of an individual for work and analyzing the mechanisms of possible changes therein in the course of long-term observation.

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ABSTRACTS OF ARTICLES FILED WITH THE ALL-UNION SCIENTIFIC RESEARCH INSTITUTE
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Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian No 1, 1981
p 96

[Abstracts]

[Text]

UDC: 577.3

"Interpolation of Biological Functions on the Basis of Discrete Data," by
A. V. Zinkovskiy, I. A. Trofimova and V. A. Chistyakov

This article deals with methods of interpolating functions specified in a discrete set of points and differentiation thereof by means of double differences of segments of Fourier series and smoothing cubic spline functions. For a practical verification of the effectiveness of the above algorithms of interpolation and differentiation, the following functions were chosen: x^2 , $\sin 2x$, $\cos x$, $e^{2x}\cos x$, e^{2x} . Twenty points were taken at interval $[0, 1]$ at a constant step of $h = 0.05$. Measurement errors were simulated with a standard MO YeS [expansion not known] 1022 program, and constituted normal dependent random values with zero mathematical expectation and mean-square error of 0.005, i.e., the error was introduced in the third significant figure of the functions under study. It was found that the spline functions provide for highest accuracy. However, if the type of function is known, one can also improve the numerical values obtained by other methods.

In an experiment conducted to determine acceleration of a free-falling body, with subsequent calculation of the second derivative on a computer, the following results were obtained: $G = 9.961 \text{ m/s}^2$ with the use of spline functions; $G = 10.834 \text{ m/s}^2$ with the method of double differences.

The proposed method for interpolation of experimental data by smoothing splines was used to solve a direct dynamics problem, i.e., to determine the controlling moments in human articulations in a specified movement. Flexion of the forearm with various aggravating factors [added weight?] was studied. This is a movement that is elementary in structure, which makes it possible to observe muscular tension as a function of its length, like a function of the articular unit, rate of contraction and magnitude of exogenous load. In addition, it is possible to check conformity of simulated data with the actual dynamics of movements and, at the same time, determine the threshold of sensitivity of the method. Equations of movement are differential second order equations with nonlinear coefficients.

Verification of accuracy of determining articular moments made it possible to demonstrate rather full coincidence of experimental and synthesized data. Experimentally, it was found that the human body develops, in the movement in question, optimum articular moments, which are the answer to a complex variational problem: determination of controlling on the basis of minimal expenditure of energy when a mechanism changes from one fixed position to another, with consideration of limitations and minimal deformations in "aggravating" and minimal deformations and oscillations at the moment it stops. The results of these mathematical and biomechanical studies revealed that it is necessary to use spline functions for mathematical processing of discrete experimental data.

UDC: 616-008.922.1-008.64-092.9:612.223.11

"Carbon Dioxide Content of Oxygen-Deficient Gas Atmosphere as a Factor in Control of Long-Term Adaptation to Hypoxia," by N. K. Khitrov, A. M. Alaverdyan, A. V. Toloknov and Ye. B. Tezikov

Conditioning rats for 21 days to a gas atmosphere with a shortage of O_2 (8-9% O_2 in N_2) under hypercapnic (4%) and normocapnic (1% CO_2) conditions leads to development of prolonged adaptation to hypoxia. Extending the conditioning period to 35 days under hypercapnic conditions disrupts adaptation; under normocapnic conditions it is retained. Adaptation is associated with moderate hypertrophy of the right ventricle, increased reserve of myocardial contractile function (RMCF), increase in hyperdynamia in response to hypoventilation hypoxia, and increase in stable reserve of norepinephrine in the heart. Impairment of adaptation is characterized by marked hypertrophy of the right ventricle, decrease in RMCF, decreased hyperdynamia of the heart with hypoventilation hypoxia, and decrease in stability of norepinephrine supply. It is concluded that graded hypercapnia during conditioning to a gas atmosphere with low O_2 content may become a means of controlling the process of long-term adaptation to hypoxia.

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